The Australian and New Zealand
JOURNAL OF SURGERY

Vol. 28 — No. 3 FEBRUARY, 1959

CARCINOMA CORPORIS UTERI

By Barry Kneale*

Royal Women's Hospital and Department of Obstetrics and Gynaecology, University of Melbourne

THE endometrium is the third most common site for malignant tumours in the female genital tract. During 1956, in the State of Victoria, breast carcinoma was five times as common as endometrial carcinoma. Carcinoma of the cervix, however, had only twice the incidence. The incidence has also increased over recent years. Of Melbourne hospital admissions in 1946 there were 34 cases out of a total of 1,802, whereas in 1956, 83 cases were reported out of a total of 3,641.

The diagnosis of endometrial carcinoma is relatively straightforward and simple. Suspicions are aroused, almost invariably, by abnormal bleeding. Curettage, followed by histological examination, is final.

Since the inception of safe anaesthesia, prognosis has been better. Few surgical statistics of recent years provide less than a 50 per cent. salvage after five years.

These factors—increasing incidence, ready diagnosis, favourable prognosis—have led to a renewed interest in the management of corporeal cancer. Radical methods of surgery and combined radio-surgical procedures have gained in popularity. It is interesting to note that, except for skin cancer, no malignant tumour offers better prospects of cure.

Material and Data

The clinical records and follow-up data of 245 patients who presented for primary treatment of corporeal cancer at The Royal Women's Hospital, Melbourne, have been analyzed. These patients presented between 1943 and 1956 inclusive.

In each case the endometrial nature of the growth was proven by histological examination of specimens obtained by curettage, laparotomy, or autopsy. Included in the series are 25 autopsy records of patients who died either before, during or after treatment.

Five patients remain untraced. Two of these were followed up regularly for a period of four years. The remaining 240 patients have been adequately traced.

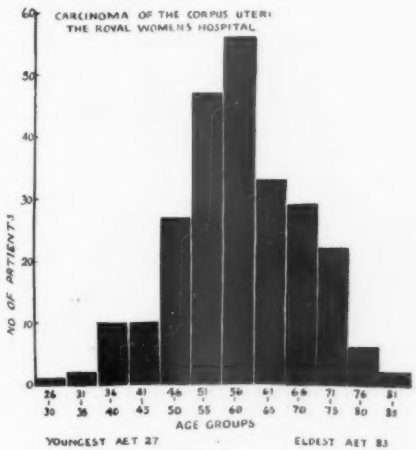


FIG. I

Age Distbibution

The accompanying graph (Fig. 1) illustrates the age distribution of patients in this series.

Noteworthy points are:—

(i) the average age of patients was 58 years,

* This work was assisted by a grant from the Anti-Cancer Council of Victoria.

(ii) all age groups between 25 and 85 have been affected,

(iii) the youngest patient was 27, the eldest 83 years.

HISTOLOGY

Table 1 depicts numerically the proportions of each histological type encountered.

Adenocarcinoma is 3 times as common as adeno-acanthoma. Squamous cell carcinoma is rare.

Corscaden (1956) quotes a 1-28 per cent. incidence of adeno-acanthoma. This represents reports from various authors.

Between 1943-1949 treatment was predominantly by intracavitary irradiation. From Fig. II it can be seen that surgical and combined radio-surgical treatment gained in popularity toward the end of the period under review.

TABLE 1

HISTOLOGY OF ENDOMETRIAL CANCER

Royal Women's Hospital, 1943-1956

Adenocarcinoma	178 cases
Adeno-acanthoma	63 „
Squamous cell carcinoma	4 „

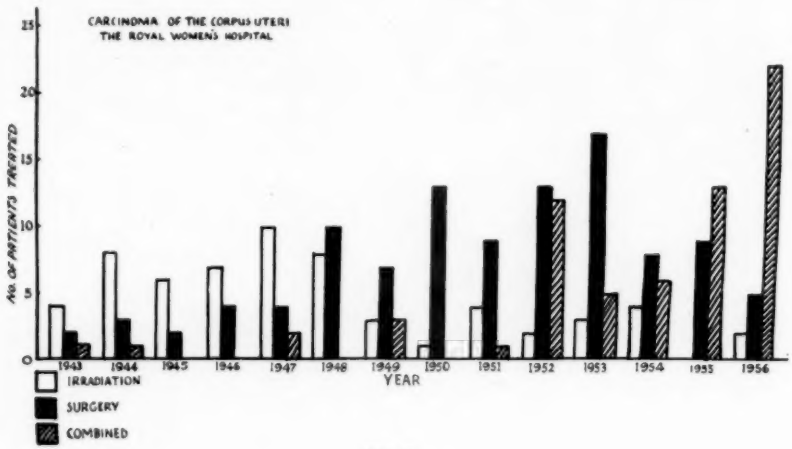


FIG II

Also he states that only 40 or more cases of squamous-cell carcinoma of the uterine body have been reported.

TREATMENT POLICY

In 1950 a Radio-Surgical clinic was formed in the Hospital. To this clinic were referred all cases of gynaecological cancer. Individual patients were seen simultaneously by a gynaecological surgeon and a radiotherapist. In each case, where applicable, treatment policy has been defined at the outset. Usually preliminary irradiation with subsequent surgery has been prescribed.

In the last five years the majority of patients with cancer has been treated in the Radio-Surgical clinic.

ANALYSIS OF TYPES OF TREATMENT

Three distinct modes of treatment have been used for operable cases:—

(1) Intracavitary irradiation.

(2) Surgical.

(3) Combined radio-therapeutic and surgical.

(1) *Intracavitary irradiation*

Technique. An intra-uterine brass tube of appropriate length is used. Its external diameter is 12.7 mm. It is designed so that its outer end projects 0.5 cm. from the cervix.

It is loaded with radon in either two or three sections depending on the length.

It provides pear-shaped isodose curves so that after six days insertion time 4650r arrives at .2 cm. through the wall of the uterus. The maximum dose received by the mucosa of fundus is between 45000 and 35000r.

Reference to Fig. II shows that this was a popular method until ten years ago. In 1956 only one patient received this treatment. Her poor general condition precluded further treatment and curettage performed four months later revealed no residual growth.

Results. In Table 2 is expressed a summary of the results obtained. Of the three post-operative deaths, two were found at autopsy to be due to perforation at radon insertion. The other death was due to general peritonitis and broncho-pneumonia.

Cancer recurrence. Three distinct factors are concerned in assessing recurrence:—

(i) Time of appearance.

(ii) Proportion of uterine recurrences.

(iii) Proportion and site of extra-uterine recurrences.

(i) In Fig. III is noted the time of death from proven cancer after irradiation. Most deaths occurred between eighteen months and two years after treatment. Few deaths arose after four years. However, there was one death at five and a half years and another at ten years. In the latter case recurrence was proven by curettage after five years, further irradiation was given, yet the patient died with generalized carcinomatosis after a further five years.

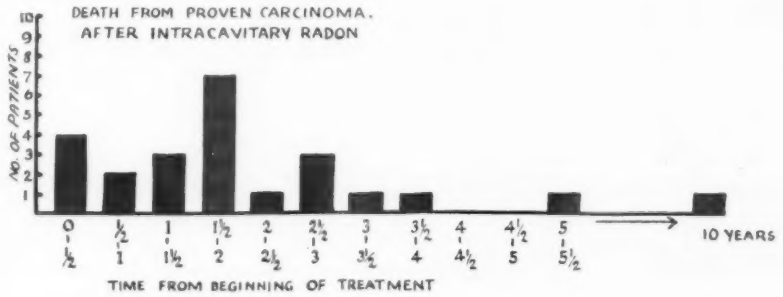


FIG. III

TABLE 2

RESULTS WITH INTRACAVITARY IRRADIATION ALONE

62 cases 1943-1956.
Average age — 60 years.
53 cases to 1952.
21 proven deaths from cancer within five years.
3 post-operative deaths.
5 years survival 20/53 = 38 per cent.
10 years survival 10/34 = 29 per cent.

There were four instances of pyometra and two cases of severe rectal stricturing.

In terms of survival, the results are quite similar to those of Heyman (1936) and Corscaden and Tovell (1954) who found an approximate 33 per cent. survival for five years with intracavitary irradiation.

(ii) These are considered under the analysis of radio-surgical treatment.

(iii) Of 22 proven recurrences, 8 occurred in the uterus, 4 were in the pelvic cavity, and in 3 patients the primary recurrence was vaginal.

Three patients returned with pulmonary metastases, 2 with ascites and one each in the abdominal wall and supraclavicular lymph nodes.

(2) *Surgical treatment*

Operability rate. How often is surgical treatment possible? Of the last 100 operable cases reviewed, 87 were considered suitable, on medical grounds, for surgical treatment.

Types of surgery employed. These have been classified as—

(A) Radical.

(B) Conservative.

(C) Inadequate.

(A) Radical Surgery.

From Fig. IV it is evident that radical surgery has been used frequently in recent years. Since 1954, where a case has been treated by surgery alone the type of surgery has usually been radical.

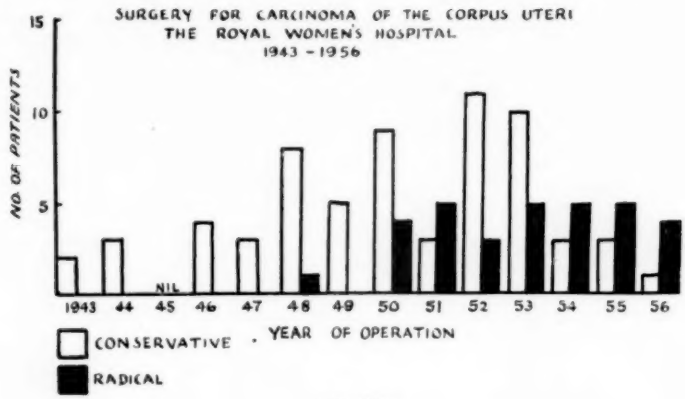


FIG. IV

In the period under review, 31 patients have been subjected to radical procedures in the following manner:—

(a) Wertheim hysterectomy .. 24 patients

(b) Radical hysterectomy (without lymphadenectomy) .. .. 4 patients

(c) Total hysterectomy (with lymphadenectomy plus adnexa .. .. 3 patients

There were two post-operative deaths (both in group (a)) and Table 3 shows a five years' salvage of 91 per cent.

(B) Conservative Surgery.

Total abdominal hysterectomy with removal of adnexa has been the standard surgical treatment for corporeal carcinoma for many years.

Results can be summarized thus:—

61 patients submitted to conservative surgery—

Operative mortality . . .	Nil
Average age	55 years
Eldest patient	83 years
Three years' survival ..	79 per cent.
Five years' survival ..	72 per cent.

(C) Inadequate Surgery.

This has been taken to include surgical excision short of total hysterectomy with removal of adnexa. This includes:—

(a) Sub-total hysterectomy,

(b) Total hysterectomy without removal of adnexa,

(c) Vaginal hysterectomy.

(a) Sub-total hysterectomy. Only two such operations have been performed. Both are alive at nine years and four years without recurrence. The former patient was not curetted prior to operation. The latter was aged 74 and extremely obese.

(b) Total hysterectomy without removal of adnexa. Only one such operation has been recorded. This patient had a papillary adenocarcinoma of the uterine cavity and was alive without recurrence four years after surgery, but has been untraced since.

(c) Vaginal hysterectomy without removal of adnexa. Three patients had this type of surgery. All are alive without recurrence at eleven, ten and four years after operation.

Bastiaanse (1952) described his results with vaginal hysterectomy for 217 cases of corporeal carcinoma. When the adnexa were removed the five years salvage was about 75 per cent. This figure decreased markedly when one or both adnexa were not removed.

In Table 4 are noted the proven primary sites of recurrence after surgery with reference to the type of surgery employed. It is apparent that conservative surgery is followed by a greater incidence of recurrence than is radical surgery, in all sites.

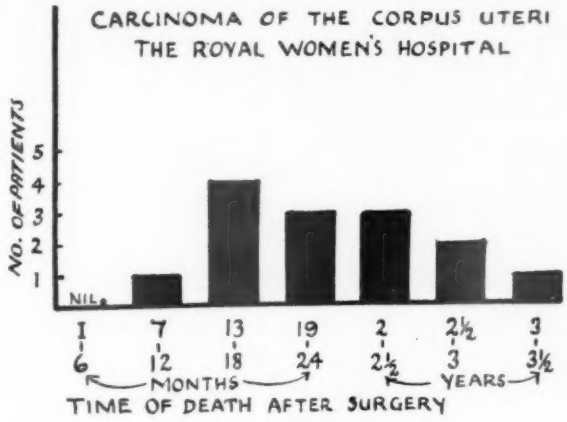


FIG. V

Incidence of cervical and adnexal spread in endometrial carcinoma.

In this series, when the whole specimen was examined in 123 cases, 93 showed no evidence of growth in the cervix or adnexa.

The cervix was invaded in 7.9 per cent. of cases. Twelve cases showed ovarian metastases—an incidence of nearly 10 per cent. Tubal invasion was demonstrable in 3 cases or 2½ per cent. In 2 cases both ovary and cervix showed invasion.

Surgical results

Ninety-eight operable patients were treated by surgery alone in this series. Of these, 51 have been treated five years or more and the survival is 77 per cent. The operative mortality has been 2 per cent. (see Table 3).

Cancer recurrence

As with irradiation one is concerned with the time, site and incidence of recurrence.

In Fig. V is represented the time of death from proven cancer after apparent curative surgical treatment. Most patients succumb between 1 and 3 years. In this series there has been no instance to date of death, after a longer interval than three and one half years.

TABLE 3

RESULTS WITH SURGERY ALONE

Five-Year Survival for Operable Cases

Inadequate surgery 3/4 = 75 per cent.		
Conservative surgery 26/36 = 72 per cent.	39/51 = 76 per cent.	
Radical surgery 10/11 = 91 per cent.		

(3) *Combined radio-therapeutic and surgical treatment.*

It is now standard practice, in the Radio-Surgical Clinic, to employ this type of treatment for carcinoma of the endometrium (see Fig. II). Naturally some cases are found to be unsuitable at one or other stage of treatment (see below).

Technique of irradiation. An intra-uterine brass tube of appropriate length is used. Its external diameter is 12.7 mm. It is designed so that its outer end projects 0.5 cm. from the cervix. It is loaded with radon in either two or three sections depending on the length. It provides pear-shaped isodose curves so that after six days' insertion time 4650r arrives at .2 cm. through the wall of the uterus. The maximum dose received by the mucosa of fundus is between 45000 and 35000r.

Surgical excision. This follows irradiation after some eight to ten weeks and may be conservative or radical.

It is important to stress that any patient regarded as being fit for surgical excision has been treated in this way since 1952.

Fifty-seven patients were planned to have this treatment. In 50 of these the plan was practicable. The reasons for break-down in treatment policy were as follows:—

(a) Irradiation refused by the patient—1 case.

(b) Inability to insert the compound intra-uterine tube—2 cases.

(c) Immediate severe local reaction to radon—1 case.

(d) Inoperable at subsequent laparotomy—3 cases.

Thus, some 12 per cent. of patients were found to be unsuitable for this type of treatment.

Randall (1951) using a similar technique found an 87 per cent. survival for five years in 98 cases.

Growth recurrence has occurred once

Case 1

Mrs. E. H., aged 60, presented in October, 1951, with corporeal adenocarcinoma. She was a diabetic, blood pressure 175/100 mm. of mercury, and in congestive heart failure with an enlarged liver and a history of angina. After medical treatment radon was inserted in February 1952 and a conservative hysterectomy was performed in May 1952. There was no residual growth in the operative specimen. However, in January 1955 a vault recurrence (well differentiated adenocarcinoma) was apparent. This was irradiated with radium needles. She was last seen in June 1957 with no evidence of carcinoma.

Residual growth. Of 52 patients irradiated, 17 patients had residual uterine growth at laparotomy and/or hysterectomy performed within three months of irradiation. Thus, approximately two-thirds showed no residual growth. Reference to Table 5 shows the response according to growth histology. The incidence of residual growth is greater in the case of adeno-acanthoma.

TABLE 4

SITES OF CANCER "RECURRENCE" AFTER SURGERY

Type of Surgery Employed	*Vagina*		*Pelvis*	*Abdomen*	*Distant Metastases*
	Vault	*Lower 1/3*			
Radical hysterectomy with node dissection (24 cases) ..	1	—	1	—	—
Radical hysterectomy (4 cases)	—	—	—	—	—
Total hysterectomy with node dissection (3 cases)	1	—	—	—	—
Total hysterectomy with removal of adnexa only (61 cases) ..	1	2	1	5	1

RESULTS WITH INTRACAVITARY RADON FOLLOWED BY CONSERVATIVE OR RADICAL HYSTERECTOMY

57 patients submitted to treatment.

7 patients excluded (see above).

Operative mortality was 4 per cent. (both patients had radical hysterectomies).

Average age was 58 years.

19 conservative hysterectomies.

31 radical hysterectomies.

19 patients initially treated three to five years ago—all alive without recurrence.

7 patients initially treated five or more years ago—all alive without recurrence.

OTHER METHODS OF RADIO-SURGICAL TREATMENT

(a) Conservative hysterectomy followed by post-operative X-ray therapy to pelvic gland fields.

This method has been used in 8 patients and only when some complicating factor has arisen. Thus, of 8 patients treated in this way, 4 were not diagnosed pre-operatively; another 3 had adeno-acanthomata or extensive growths, and one was a patient with an ovarian metastasis. The five years' survival has been 63 per cent.

(b) Conservative hysterectomy followed by radon application to the vaginal vault.

Seven patients received this type of the treatment and the five years' survival was 67 per cent. Two patients were undiagnosed prior to surgery; 2 had an extensive growth through the uterus, and one had an ovarian metastasis.

TABLE 5

RELATIONSHIP OF RESIDUAL GROWTH TO HISTOLOGY

	Number Irradiated	*Residual Growth*
Adenocarcinoma	40	11
Squamous cell carcinoma	2	1
Adeno-acanthoma	10	5

THE MANAGEMENT OF INOPERABLE CARCINOMA OF THE ENDOMETRIUM

These patients were encountered as follows:—

1. *Inoperable on clinical findings.*

Twelve patients in the whole series, i.e., 5 per cent., were found initially to be inoperable. Only 3 criteria were accepted for inoperability:—

(a) the presence of vaginal metastases—4 patients,

(b) the presence of a "frozen" pelvis—4 patients.

(c) Cachexia and/or distant metastases—4 patients.

(a) Vaginal metastases.

One patient survived fourteen months following irradiation and Wertheim hysterectomy. Death was due to uraemia and there was no evidence of carcinoma at autopsy. One patient survived two years following a Wertheim hysterectomy. Two months post-operatively there was a vaginal recurrence. The patient refused irradiation. One patient lived seven weeks. She presented with a haemoglobin of 19 per cent. and the vaginal vault filled with carcinoma. Blood transfusion was given but she died of uraemia. At autopsy the carcinoma extended throughout the pelvis. The last patient presented with vaginal metastases which proved to be adeno-acanthoma. These were irradiated and she died two years later from pulmonary metastases but with no pelvic recurrence.

(b) "Frozen" pelvis.

In each case it was confirmed at laparotomy that the patient was inoperable. The average duration of life from the first visit was 2 months.

(c) Cachexia and/or distant metastases.

One patient presented with malignant ascites, one with oedema of the vulva and gross anaemia, and the other two with gross anaemia and congestive cardiac failure. All patients died within three months.

2. *Inoperable at laparotomy.*

One hundred and thirteen patients were submitted to laparotomy as a primary procedure, and 8 of these were found to be inoperable. In 2 patients growth had extended into the round ligaments, parametrium and uterovesical or recto-uterine peritoneal pouches. One patient had an irremovable mass in the greater omentum. 3 patients had tumour nodules over the peritoneal surface of the uterus. In one instance, there was invasion of the broad ligament and sigmoid. In another, the growth extended through the uterus to the lateral pelvic wall. One patient had carcinomatosis peritonei.

Associated inoperable growths.

One patient had inoperable carcinoma of the sigmoid colon, another had a uterine sarcoma and carcinoma of the cervix and another had an inoperable papillary cystadenocarcinoma of the right tube and ovary.

PALLIATIVE SURGERY AND/OR RADIOTHERAPY

The following 2 cases illustrate the value of palliative treatment:—

Case 2

Mrs. J. A., aged 41, presented in March 1955 with three separate primary growths—fundus uteri, right Fallopian tube and right ovary. There were implants in the pouch of Douglas. Palliative Wertheim hysterectomy was performed. In August 1956 a pelvic recurrence was noted and deep X-ray therapy was given. In February 1957 the patient had intestinal obstruction together with liver and mesenteric metastases. She died at the end of June 1957, some two years and three months after palliative treatment was begun.

Case 3

Mrs. D. R., aged 59, presented in June 1953 with a carcinoma corpus uteri presenting at the cervix. Laparotomy revealed the left Fallopian tube filled with growth and attached to ileum, colon and greater omentum. Palliative left salpingectomy was performed and post-operative palliative deep X-ray therapy was given.

In November 1955 it was found that the patient had a pelvic mass and a radical hysterectomy was performed. The left ovary contained adeno-acanthomatous deposits as did the entire uterus. In May 1956 a vault recurrence was irradiated. In June 1957 a small bowel obstruction was relieved. This was due to extrinsic growth attached to the abdominal wall. The patient is now still alive and seemingly well more than four years after the beginning of palliative treatment.

Excluding Case 2 the average duration of life in patients inoperable at laparotomy was eight and one half months.

(i) *Operative mortality.*

There have been 58 Wertheim operations performed for carcinoma corporis uteri between 1943 and 1956, with 4 post-operative deaths. Thus, the operative mortality has been approximately 7 per cent. In 3 of the 4 cases who succumbed operative difficulties were encountered. In 3 cases death was due to pulmonary embolism, and the other patient died following a massive intra- and retroperitoneal haemorrhage.

TABLE 6

LYMPH NODE METASTASES AT LYMPHADENECTOMY

Patient	*Histology*	*Previous Radiotherapy*	*Uterine Pathology*	*Sites of Metastases*	*Result*
(1) Mrs. M.M. aged 46 B.33924	Immature adeno-acanthoma	Intracavitary radon	Isthmical residual carcinoma almost through wall	R. common iliac R. internal iliac	Alive five years
(2) Mrs. M.M. Aged 66 B.38862	Papillary adeno-acanthoma	Intracavitary radon	No residual carcinoma of uterus	R. common iliac R. obturator L. obturator	Alive three years and ten months
(3) Mrs. S.W. Aged 49 B.44516	Moderately well differentiated papillary adenocarcinoma	Intracavitary radon removed at 20 hours due to peritonitis	Extensive papillary adenocarcinoma fundus to internal os with deep invasion of the wall	R. obturator L. obturator	Alive two and one half years
(4) Mrs. E.B. Aged 64 B.52902	Not well differentiated squamous cell carcinoma	Intracavitary radon and vault ovoids	Squamous carcinoma at the fundus well into the wall	L. common iliac	Post-operative death due to massive pulmonary embolism

TREATMENT REFUSED BY THE PATIENT

Occasionally one encounters opposition to irradiation and/or surgery. In 2 cases all treatment was refused.

Case 4

Mrs. L. McG., aged 80, presented in March 1955 with a procidentia and papillary adenocarcinoma of the uterine body diagnosed by curettage. In January 1957 the carcinoma was noted to have extended to the external os and was of the same histology.

Case 5.

Mrs. R. K., aged 78, presented in January 1951 with an adeno-acanthoma of the corpus uteri diagnosed by curettage. She refused all treatment and died in August 1952.

WERTHEIM HYSTERECTOMY IN THE MANAGEMENT OF CARCINOMA CORPORIS UTERI

One may now survey critically the collective experiences of this hospital.

Hence the elderly, obese patient who typically suffers from this type of cancer offers technical difficulties which may modify a radical procedure at short notice.

Hawksworth (1954) quotes a mortality of nearly 6 per cent. at Oxford whilst Rickford (1954) in a short series of 17 cases had 2 post-operative deaths. Winterton (1954) described an operative mortality of 3.5 per cent. in a series of 90 cases.

(ii) *Urological complications*

Forty-one of the 58 cases were subjected to close scrutiny by routine serial post-operative excretory pyelograms (Godfrey and Macdonald 1957). The technique employed is that of performing a pre-operative pyelogram in each case. This is repeated after operation immediately prior to the patient's discharge from hospital. If there is any abnormality, the films are taken at upwards of monthly intervals and interpreted in conjunction with full urological investigation.

Patients with normal pyelograms are checked approximately at three, six and twelve months, then at yearly intervals. Recently Macdonald has been employing a single film taken twenty minutes after dye injection.

Three patients developed uretero-vaginal fistulae and in two of these surgery was preceded by irradiation. One non-functioning kidney and 6 persistent unilateral hydronephrosis have been discovered.

(iii) *Lymph node metastases*

Four instances of positive nodes were detected in a series of 61 cases where nodes were available for histological examination. This is an incidence of approximately 7 per cent. The nodes involved, in order of frequency, were (a) common iliac, (b) obturator and (c) internal iliac (see Table 6).

Javert (1952) found a 28 per cent. incidence of node involvement in 50 cases. The 5 years survival in such cases was 28.5 per cent. Liu and Meigs (1956) found an incidence of 23 per cent. in 47 cases subjected to lymphadenectomy. Recently Godfrey (1957) has been extending the lymphadenectomy to a radical post-rectal clearance.

Autopsy findings. Additional information has been gained from the autopsies of 25 patients who had received all types of treatment. There were 4 instances of lymph node metastases which is an incidence of 16 per cent. All 4 had para-aortic lymph node invasion, and of these one had concomitant metastases in mediastinal, iliac and inguinal lymph nodes. All patients had widespread metastases in other organs. Two of the patients were inoperable at original laparotomy and the other two had had previous conservative hysterectomies.

SUMMARY

(1) Corporeal carcinoma is shown to have a rising incidence.

(2) Two hundred and forty-five cases of proven carcinoma corporis uteri presented at the Royal Women's Hospital, Melbourne, between 1943 and 1956, for primary treatment.

(3) The average age of the patient was 58 years but ages varied between 27 and 83 years.

(4) A 25 per cent. incidence of adeno-acanthoma is noted in this material.

(5) The growth of a Radio-Surgical clinic staffed by gynaecologists and radiotherapists has led to combined treatment for most cases since 1950.

(6) Treatment by intracavitary irradiation has resulted in a 38 per cent. five years survival. Death from carcinoma has occurred sporadically up to ten years after treatment.

(7) Surgery has been possible in 90 per cent. of patients.

(8) Five years survival with conservative surgery is about 70 per cent. Death from carcinoma has occurred invariably within three years after treatment.

(9) Inadequate surgery, particularly vaginal hysterectomy, has been shown to give fair results in a very limited number of patients.

(10) Preliminary intracavitary irradiation and subsequent surgery has yielded no death from carcinoma to date and one case of growth recurrence.

(11) Residual growth occurs in the uterus in one-third of cases. Radio resistance occurs more often with adeno-acanthoma.

(12) Hysterectomy followed by X-ray therapy or vault irradiation has yielded fair results in a small selected group of cases.

(13) Criteria for inoperable growths include vaginal metastases, a "frozen" pelvis or cachexia and/or distant metastases. Palliative surgery has been found to be of benefit in some cases and one patient has survived five years.

(14) Wertheim hysterectomy has been used in 58 patients with carcinoma corporis uteri. The operative mortality has been 7 per cent. and lymph node metastases much the same figure. The incidence of urological complications is much lower than that seen in similar surgery for cervical cancer.

(15) Lymph node metastases seen at autopsy have been predominantly para-aortic.

CONCLUSIONS

(1) Operation in "inoperable" cases often palliates suffering to a marked extent and prolongs survival.

(2) Irradiation alone should be reserved for the exceptionally ill or enfeebled patient.

(3) Radio-surgical treatment is warranted on the basis of results in all other cases. In a very few, technical difficulties prevent irradiation or subsequent surgery may prove a case inoperable.

(4) Radical surgery must be carefully considered both pre-operatively and at operation. It seems likely that there will be a greater incidence of lymph node involvement in growths presenting at the cervix, extensively invading the uterus or exhibiting squamous differentiation.

ACKNOWLEDGEMENTS

My particular thanks are due to the Honorary Medical Staff of The Royal Women's Hospital, Melbourne, for their permission to investigate and report upon these cases.

Mr. Graham Godfrey and Dr. Arthur Hill have proved a constant source of information and enthusiasm. Dr. Robert Barter, Acting Director of the King George V Department of Pathology, has offered invaluable criticism and help. Dr. W. P. Holman, Medical Director of Peter MacCallum Clinic has supplied the technical details of radiotherapy.

Finally, my sincere thanks are due to Mrs. Barker and Miss Johnson for their labour in preparation of the tables and the photography.

REFERENCES

ANTI-CANCER COUNCIL OF VICTORIA (1946, 1956), "Statement of Metropolitan Hospital Admissions".

BASTIAANSE, M. A. (1952), *J. Obstet. Gynaec. Brit. Emp.*, vol. 59, page 611.

CORSCADEN, J. A. (1956), "Gynaecological Cancer", 2nd Edition, Baltimore, Williams and Wilkins, page 386.

—— and TOVELL, H. M. M. (1954), *Amer. J. Obstet. Gynec.*, vol. 68, page 737.

CUSCADEN, W. G., and ODDIE, T. H. (1939), *J. Obstet. Gynaec. Brit. Emp.*, vol. 46, page 289.

GODFREY, G. (1957), Personal communication.

—— and MACDONALD, C. (1958)—In preparation.

HAWKSWORTH, W. (1954), *Proc. roy. Soc. Med.*, vol. 47, page 905.

HEYMAN, J. (1936), *J. Obstet. Gynaec. Brit. Emp.*, vol. 43, page 655.

JAVERT, C. T. (1952), *Amer. J. Obstet. Gynec.*, vol. 64, page 780.

LIU, W., and MEIGS, J. V. (1956), *Amer. J. Obstet. Gynec.*, vol. 69, page 1.

MACDONALD, C. (1957), Personal communication.

RANDALL, J. H., MIRICK, D. F., and WIEBEN, E. E. (1951), *Amer. J. Obstet. Gynec.*, vol. 61, page 596.

RICKFORD, R. (1954), *Proc. roy. Soc. Med.*, vol. 47, page 899.

WINTERTON, W. (1954), *Proc. roy, Soc. Med.*, vol. 47, page 897.

SPORADIC AMOEBIASIS IN VICTORIA

By A. M. Cuthbertson and J. D. Tange

Department of Pathology, University of Melbourne

AMOEBIASIS was first reported in Australia by Fiaschi (1898) and Isbister (1898), the infection probably being contracted in the New Hebrides. Soon afterwards, a case was recorded in a police trooper who had been stationed for some time in the Northern Territory but who had not lived abroad (Verco, 1899). Other examples were noted in mining communities (Isbister, 1899; O'Brien, 1899; Goldsmith, 1902), and in 8 of 23 patients dying of liver abscess at the Sydney Hospital between 1892 and 1898, there was ulceration of the large intestine (Isbister, 1899). Another patient with hepatic amoebiasis may have been infected in a mining area (Corlette, 1915). Cases were also noted in men who had served in the Boer War (Nelson and Shearman, 1918; Dew, 1921) and in relatives (Colville, 1922; Patterson, 1923) or workmates of ex-servicemen (Baldwin, Heydon and Broben, 1927).

The parasite has been isolated from the stools of approximately one per cent. of persons examined in Townsville, North Queensland (Willis, 1923), of troops without overseas service (Bearup, Lawrence and Heydon, 1949; Lancaster, 1953) and of Sydney children (Bearup *et alii*). In the district around Townsville about 4 per cent. of persons examined were found to carry *E. histolytica* (Maplestone, 1921). Cowling and Plunkett (1958) have isolated the parasite from 6 per cent. of patients attending the Royal Melbourne Hospital with gastro-intestinal complaints. In these investigations, the procedure adopted generally comprised the examination of a single stool.

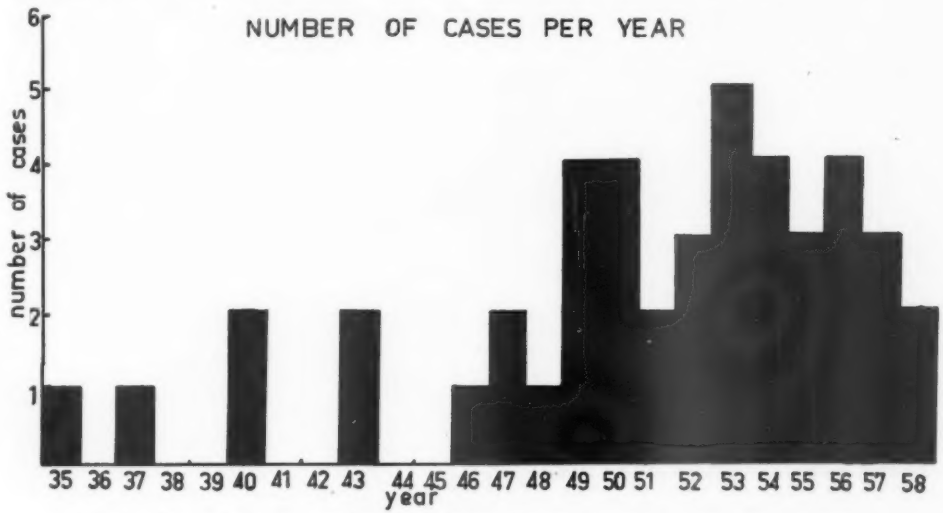


FIG. I. The incidence of amoebiasis in Melbourne teaching hospitals between 1935 and 1958.

Over the past twenty-four years, and especially during the last decade, a number of patients suffering from amoebiasis has been admitted to Melbourne teaching hospitals; these have been studied in order to demonstrate the pattern of the disease as it occurs in Australia.

Material

The group consists of 44 patients admitted to Melbourne teaching hospitals between 1935 and 1958 (Fig. I).

There were 40 males and 4 females; their ages ranging between 16 and 75 years (Fig. II); 12 of these patients had never lived outside of Australia (Fig. III). In 13 information on this point was unavailable (2 of these patients had been referred from mental hospitals) and of the remaining 19, 11 were ex-servicemen, (one, a Boer War veteran presented in 1940); 3 had travelled abroad, and 5 were migrants. Some had been twenty years or more in Australia before developing symptoms. Twenty-two patients had colitis alone, 13 had hepatitis, and 9 some other complication.

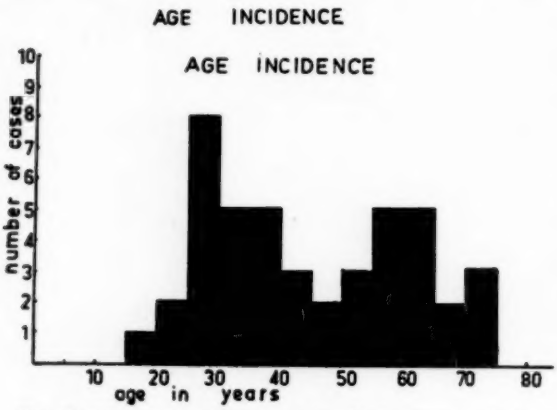


FIG. II. The relative frequency of amoebiasis among patients of different age groups.

The diagnosis was made by the demonstrations of the parasite in discharges or tissues and by the response to specific therapy.

Patients who entered the country with active amoebic infection were excluded.

CLINICAL AND PATHOLOGICAL FEATURES

Colitis

The patients all complained of diarrhoea, usually intermittent and often of long duration, in one case for eighteen years. The motions were often fluid, especially in exacerbations, though they might sometimes be soft and semi-formed. Blood and mucus were present constantly or intermittently. Very occasionally, the diarrhoea was abrupt, intense and of short duration. Lower abdominal pain relieved by defaecation was not uncommon, and tenesmus accompanied severe lesions in the rectosigmoid. Weight loss was by no means invariable. There may have been some abdominal tenderness, especially in one or other iliac fossa, but more often examination showed no such feature. A neutrophil leucocytosis was a frequent feature but eosinophilia was much less common. The temperature was sometimes normal and pyrexia greater than 101° Fahrenheit was associated with some complication such as invasion of the liver or bronchopneumonia.

The typical sigmoidoscopic appearances were small or confluent ulcers with a raised hyperaemic margin and a sunken yellow base. The intervening mucosa was normal or oedematous but might be friable and bleed easily, a phenomenon observed even in the absence of ulceration. Sometimes the lesions were situated beyond the reach of the sigmoidoscope. Barium enemata were usually normal; in 2 patients the appearances of loss of haustrations of the colon (Fig. IV) led to a provisional diagnosis of ulcerative colitis.

Case 7

A 67 year old male had suffered intermittent diarrhoea, with blood and mucus in the stools, for eight years, losing 2 stone in weight. He was tender

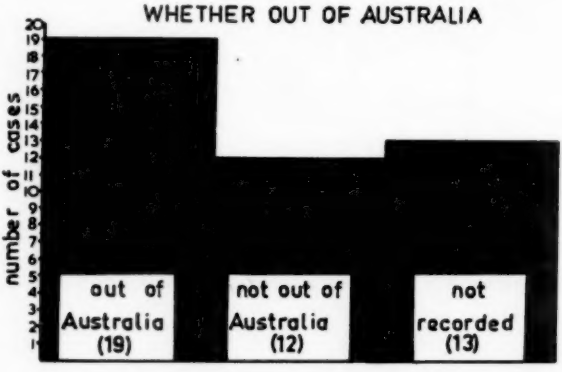


FIG. III. The domiciliary history of 44 patients suffering from amoebiasis.

in the right iliac fossa and sigmoidoscopy showed shallow ulcers with a greyish yellow base, and raised red edges; the intervening mucosa was a dull deep red. Loss of haustrations of the colon was demonstrated by the barium enema. Amoebae were present in the faeces and there was a rapid response to the emetine.

In one patient the disease complicated pregnancy.

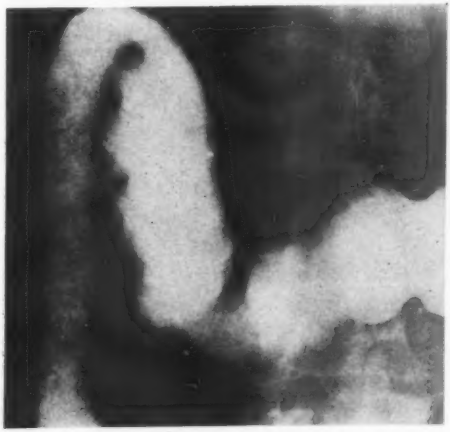


FIG. IV. X-ray photograph of the ascending colon of a patient with amoebiasis showing loss of haustrations.

Case 15

A 28 year old female complained of dragging pain in the pelvis in the last months of pregnancy; an episode of bleeding from the rectum culminated in a successful delivery at thirty-six weeks. An anaerobic streptococcal infection in the puerperium was overcome with chemotherapy but the rectal bleeding continued and was accompanied by profuse diarrhoea and eventually dehydration. An indurated bleeding ulcer was found on rectal examination and proctoscopy and amoebae were isolated from the stools. Despite emetine, her temperature rose to 101.5° Fahrenheit and her liver enlarged and became tender. She responded rapidly to aureomycin and continued to improve during a second course of amoebicidal drugs.

In two elderly patients severe diarrhoea was associated with coronary artery thrombosis and a fatal myocardial infarction.

Case 34

A 75 year old female who had never lived outside Australia had been troubled by intermittent diarrhoea for ten years; for one week it had been profuse and blood stained. She looked ill and proctoscopy showed many small ulcers separated by hyperaemic mucosa. Amoebae were present in the stools. The patient died suddenly soon after admission. At autopsy, flask-shaped ulcers with a hyperaemic border were distributed throughout the entire colon. There was a recent thrombus in the right coronary artery and an extensive posterior myocardial infarct which had ruptured.

Perforation of the colon occurred in 4 patients, in 2 of whom perforation of the sigmoid colon was followed by a fatal general peritonitis.

Case 3

A 41 year old diabetic male suffered from diarrhoea and fever after haemorrhoidectomy. One month later, drainage of a right subphrenic abscess was carried out but his diarrhoea continued for six weeks, when signs of peritonitis developed. He died twenty-four hours after laparotomy. Repeated examinations had failed to reveal amoebae in the stools.

At autopsy, the colon was oedematous and ulcerated from the sigmoid to the caecum and there was a large perforation in the sigmoid. There was a large abscess in the right lobe of the liver. Amoebae were present in sections of both colon and liver.

One patient with a pericolic abscess subsequently developed a cerebral abscess.

Case 24

A 52 year old labourer was treated for a pericolic abscess by segmental excision of the transverse colon and end to end anastomosis. The wound discharged for five months, though no faecal fistula was demonstrated. A large abdominal wall abscess was then drained and amoebae identified in the discharge. He improved remarkably after a course of anti-amoebic drugs, including carbasone. He then developed neurological signs which were thought to be possibly due to arsenic poisoning but there was no improvement following a course of B.A.L. Two weeks later signs of a left hemiplegia appeared. He died twenty-four hours after aspiration of cerebral abscess.

At autopsy, there was a large honey-combed abscess in the abdominal wall, which did not communicate with the bowel and an extensive cerebral abscess in the right temporal and parietal lobes. Amoebae were found only in the abdominal wall abscess.

In one patient a perinephric abscess followed perforation of the caecum.

Case 38

A 16 year old patient, the brother of several exservicemen, developed fever, recurrent pain in the left iliac fossa and diarrhoea. At laparotomy, a large mass was seen in the mesentery and his appendix was removed. His fever slowly subsided and the mass disappeared but he lost 3½ stone in weight, the wound taking nearly six months to heal; meanwhile he experienced anorexia, nausea, diarrhoea and pain in the right iliac fossa. A barium enema showed some narrowing of the caecum. These symptoms

recurred over the next ten years and there was occasional blood in his motions. Eventually the pain became continuous, a lump appeared in the right loin and a perinephric abscess, which communicated with the caecum, was drained. A right hemicolectomy was subsequently performed to close the fistula but the wound broke down and the fistula was re-established.

After repeated attempts amoebae were identified in the discharges and a slow but definite improvement followed emetine therapy.

One year later under emetine cover, the area of the original anastomosis was resected and the continuity of the bowel restored.

Another patient, known to have a peptic ulcer, presented with malaena and signs suggesting perforation.

Case 39

A 74 year old male experienced low back pain for five weeks and diarrhoea for two days. He was confused and dehydrated and his abdomen rigid and tender. He passed two melaena stools after admission. At laparotomy there was foul smelling fluid in the peritoneal cavity, and the transverse colon appeared thickened, inflamed and oedematous.

A high gastric ulcer was also found. The patient died shortly afterwards.

At autopsy there was a chronic gastric ulcer on the lesser curvature 2 cm. below the cardia. The whole of the colon was oedematous and inflamed and the mucosa ulcerated; amoebae were found on microscopic examination.

There was one other fatality in this group, a Boer War veteran, whose illness was complicated by a severe broncho-pneumonia. In all, 7 of 27 patients died of their disease.

PATHOLOGICAL FEATURES

Amoebic infection involves the large, never the small bowel. The lesions may be situated only in one region, sometimes in the caecum and the ascending colon; sigmoidoscopy may thus be negative.

Circumscribed areas of the epithelium are replaced by yellow collections of inflammatory cells. From this focus the invasion proceeds in the submucosa beneath intact epithelium (Fig. V) so that the edges of the ulcers are raised and hyperaemic. The ulcers may remain separate or spread in the transverse axis, becoming confluent. Spread may be confined to the submucosa, or continue through the muscle to the serosa (Fig. VI). The intervening mucosa is usually normal but may show some degree of inflammatory cell infiltration.

Hepatic amoebiasis

The clinical manifestations followed a well defined pattern; for a month or more the patient noticed a lassitude and malaise, though these premonitory symptoms were not invariable. Then followed attacks of sweating and shivering, which seemed to be endured for about three weeks before medical advice was sought. Deep, aching pain was felt under the right costal margin or in the epigastrium and rarely around the right shoulder. Occasionally there were episodes of vomiting; diarrhoea was an inconstant symptom and usually not troublesome.

FIG. V. Photomicrograph of a section of the colon of a patient with amoebiasis showing inflammation extending beneath intact mucosa at the edge of an ulcer. Haematoxylin and eosin stain. (x 30)

The liver was found to be enlarged and tender. Sigmoidoscopic examination was usually normal and amoebae were found only infrequently in the stools. Diagnosis then depended upon a clear response to emetine therapy. On screening, the right hemidiaphragm was found to be elevated and its movement restricted. One patient, with a negative Casoni test, showed calcification in the liver. In only one patient was there a pleural effusion. Often but not always there was a neutrophil leucocytosis and the temperature rarely exceeded 101° Fahrenheit.

In 4 patients there was rupture of a liver abscess. In 2 patients peritonitis resulted and in one this was the first of a series of complications.

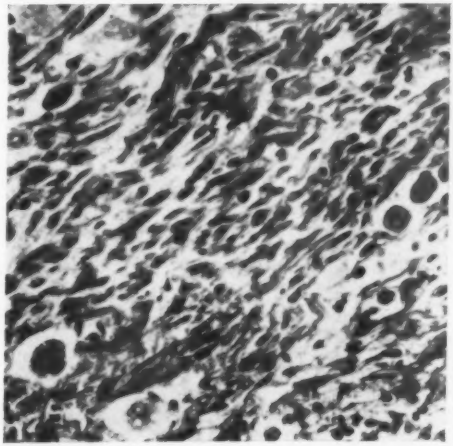


FIG. VI. Photomicrograph showing amoebae infiltrating oedematous smooth muscle in the wall of the colon. Haematoxylin and eosin stain. (x 400)

Case 14

A 35 year old ex-serviceman, who had suffered 2 attacks of dysentery overseas six years previously and a further attack five years later and who had for many years experienced post-prandial epigastric pain relieved by alkalis, developed increasingly severe abdominal pain. On admission nine days later he was found to have a rigid and tender abdomen, especially in the epigastrium and right iliac fossa. At laparotomy there was clear fluid and plaques of fibrin in the upper abdomen. The wound was drained and discharged blood and pus. Three weeks afterwards a tender mass formed in the right loin and pustules appeared over the trunk; these later formed indolent ulcers. He died suddenly after passing 3 large melaena stools.

At autopsy, there were abscesses between the upper pole of the right kidney and the under surface of the liver, in the pelvis, and around a perforation in the lateral wall of the caecum. The first of these communicated with a multilocular, thick-walled abscess in the right lobe of the liver. Amoebae were found in the pus. In the colon were numerous shallow anastomosing ulcers with hyperaemic borders. The intervening mucosa was normal.

In the other two patients the rupture occurred on the superior surface of the liver, through the diaphragm, into the substance of the lung; in both instances involvement of the lung was manifested by haemoptysis. The first patient recovered after drainage of an empyema.

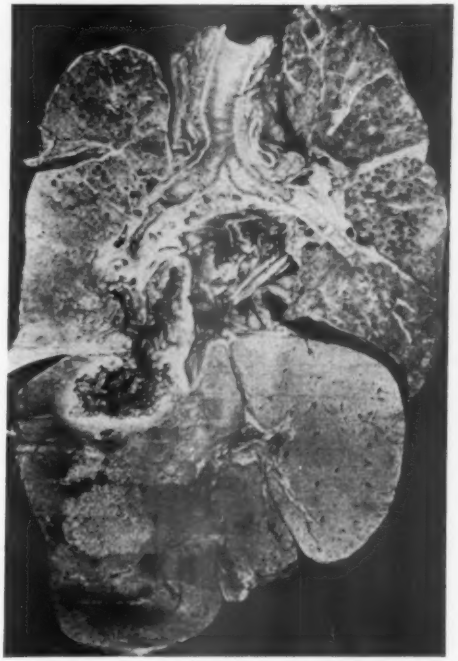


FIG. VII. A large thick-walled abscess in the right lobe of the liver extending across the diaphragm into the lung.

Case 13

At laparotomy, a 52 year old male with intermittent diarrhoea was found to show thickening and nodularity of the whole of the sigmoid, transverse, and ascending colon. There was no tumour deposit in the corresponding lymph nodes. His diarrhoea continued, and four years later he developed right-sided chest pain, dyspnoea, haemoptysis, and loss of weight. A right-sided empyema was present and at operation a large liver abscess was found to have ruptured through the diaphragm, which had almost sloughed away, into the right lung. Amoebae were found in scrapings of the wall of the abscess but not in the pus. Anti-amoebic therapy was begun; convalescence was uneventful.

In the second patient the course of the illness did not suggest the presence of a lesion outside the lungs.

Case 11

A 62 year old male suffered haemoptysis for two weeks. Abnormal physical signs were not present, but bronchoscopy showed blood coming from the

right lung. A bronchogram showed minimal bronchiectatic changes but the radiologist noted that thick, opaque, reddish brown sputum was produced during the examination. A right-sided empyema was drained but he died two days later.

At autopsy there was a liver abscess with amoebae in its wall, extending through the diaphragm into the lung.

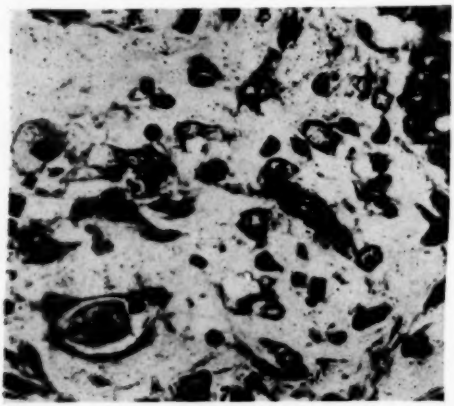


FIG. VIII. Photomicrograph of the wall of a liver abscess showing granulation tissue, fragments of biliary epithelium, an amoeba in a vessel and, above this, portion of a liver cell. Iron haematoxylin stain. (x 650)

Pathological appearances

The abscesses are multiple and may be limited by a thick connective tissue wall (Fig. VII), infiltrated with inflammatory cells and containing bile ducts and occasional liver cells (Fig. VIII). The surrounding liver tissue is then normal though the connective tissue in the portal tracts may be increased. Areas of liver cell necrosis may be demarcated from surrounding liver tissue only by a border of inflammatory cells or by a narrow layer of recently formed connective tissue (Fig. IX). The liver trabeculae are damaged and surrounded by congested sinusoids. Cells adjoining the portal tracts are relatively normal. In these circumstances amoebae may be found in damaged liver tissue (Fig. X); when a well formed connective tissue wall is present, they are found in its inner layers (Fig. XI).

Cerebral amoebiasis

One patient (Case 24) developed a cerebral abscess at a time when an amoebic abscess of the abdominal wall was healing.

Amoebae were not isolated from the pus, and could not be found on microscopic examination which demonstrated multiple pyogenic abscess formation, thromboses in the vessels, and areas of cerebral necrosis.

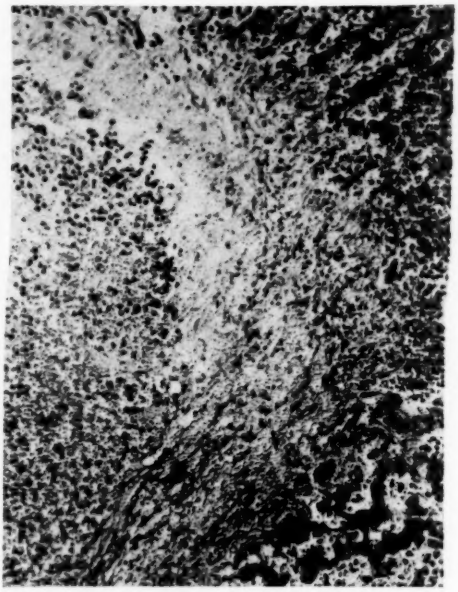


FIG. IX. Photomicrograph of portion of the liver, showing an abscess with a loose connective tissue wall. The surrounding liver cells are damaged and the sinusoids congested. Haematoxylin and eosin stain. (x 100)

Cutaneous amoebiasis

Three patients developed skin lesions. In Cases 21 and 38, the lesions were situated around a fistula. Case 21 showing rapid necrosis of the skin has previously been reported (Shaw and Hughes, 1951).

In the third patient, Case 14, lesions appeared over the trunk; however, in the absence of histological material it is impossible to prove systemic amoebic infection of the skin.

The inflammatory process spreads beneath intact epithelium (Fig. XIII); at the base of the lesion granulation tissue is formed.

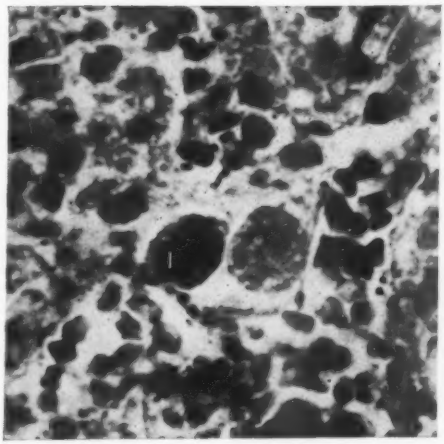


FIG. X. Photomicrograph of portion of the liver showing damaged liver cells and amoebae adjacent to a congested sinusoid. Picro-Gomori stain. (x 1000)

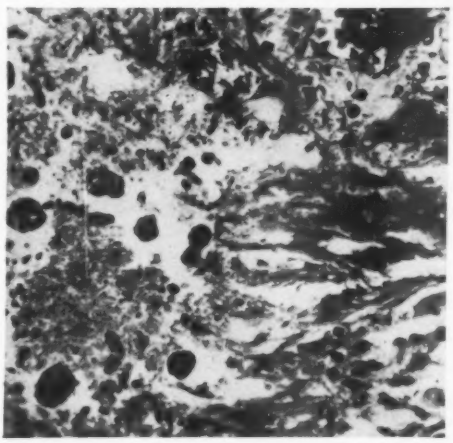


FIG. XI. Photomicrograph of portion of the wall of a liver abscess showing amoebae in its inner layers. Picro-Gomori stain. (x 400)

DISCUSSION

The high mortality (25 per cent.) and the high incidence of complications (20 per cent.) in these patients is in excess of that in other series (Rives, Heibner and Powell, 1955). These writers noted complications (other than liver abscess) in 12 of 1,062 patients with amoebic colitis in New Orleans.

This reflects difficulty in diagnosis and consequent delay in treatment, a situation due sometimes to the patient's failure to seek medical advice early in his illness and sometimes to a failure to identify the parasite on one or more occasions. This recalls the failure to establish the diagnosis ante-mortem in 66 per cent. of patients of one series of 148 fatal cases (Kean, Gilmore and Van Stone, 1956). A single stool examination is only 20 per cent. efficient in diagnosis, and examination of 3 stools on consecutive days, only 60 per cent. efficient. Purgation increases the likelihood of finding amoebae in a particular specimen but reduces it for some days subsequently. Examination of material aspirated at a sigmoidoscopy, even in the absence of ulceration, further enhances the prospects of success (Sodeman, 1952). It will be recalled

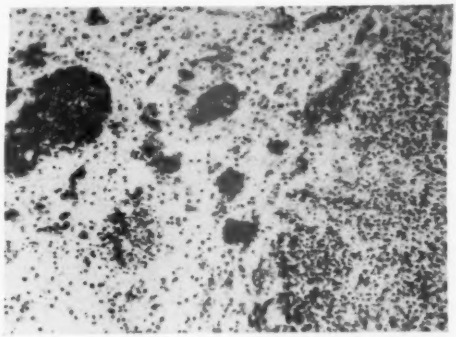


FIG. XII. Photomicrograph of the brain showing portion of a cerebral abscess, thrombi in adjacent vessels, and inflammatory cell infiltration of both the thrombi and the cerebral tissue. Haematoxylin and eosin stain. (x 75).

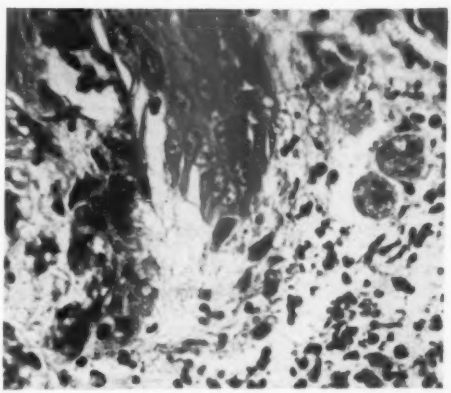


FIG. XIII. Photomicrograph of portion of the skin showing amoebae beneath intact epithelium. Picro-Gomori stain. (x 500)

that Australian investigations into the frequency of amoebic infestation have been carried out upon the basis of examination of a single stool and may in consequence underestimate its true incidence. In the present series, diagnosis depended on demonstration of amoebae in stools, discharges or tissues or upon the response to emetine; culture (Radke, 1953) or the complement fixation test (Hall and Carruthers, 1957) were not employed.

While the clinical picture conforms to a well defined, though not distinctive, pattern there are exceptional cases in which the course of the disease is short and fulminating (Kean *et alii*) or in which the most characteristic symptom, diarrhoea, is absent or mild and fleeting (Davies, 1955). Physical examination is usually negative, and when the lesions are confined to the right side of the colon, sigmoidoscopy will be normal. The radiological changes observed are not diagnostic of amoebiasis which, however, should be suspected when changes such as irregularity of outline are localized to the caecum and ascending colon or if there is a conical deformity of the caecum (Davies). The appearances should resolve with therapy. Awareness is the most important factor in diagnosis, for amoebiasis may mimic acute appendicitis, peptic ulcer, empyema, ulcerative colitis and carcinoma of the large bowel.

One complication of amoebic infection of the colon, pronounced connective tissue formation which constitutes the amoebic granuloma with formation of a stricture or a mass, was not demonstrated in these patients. Complications noted were perforations with generalized or localized peritonitis, haemorrhage, infection of the liver, skin and possibly the brain.

Hepatic amoebiasis is characterized by focal necrosis, followed by abscess formation, and in the early stages by damage to surrounding liver tissue. Diffuse amoebic hepatitis has not been demonstrated (Kean, 1955). Both circulatory and allergic factors may contribute to the establishment of amoebic infections of the liver (Lamont and Pooler, 1958). Guinea pigs have been shown to be much less resistent to intravenous infection with *Entamoeba histolytica*, when colitis is already present (Maegraith and Harinasuta, 1953). Moreover, as these investigators point out, the problem is further complicated in both its clinical and experimental aspects by the possibility of coincident bacterial infections.

The clinical features of hepatic involvement in this series approximate to those described in a comprehensive study of this complication (Ochsner and DeBakey, 1943). Jaundice was not encountered; when present it has been ascribed to obstruction of the biliary passages by a large abscess (Lamont and Pooler) or to parenchymal damage (Kean *et alii*). These workers observed jaundice in the absence of hepatic amoebiasis in patients with severe colitis. It has been suggested that leucocytosis is more likely with a short, and anaemia with a long, history (Lamont and Pooler).

Rupture into the peritoneum and across the diaphragm into the lung was noted in 4 patients. The prognosis of the second complication is improved by free drainage through a bronchial fistula (Ochsner and DeBakey). Rupture into the pericardium did not occur.

Cutaneous involvement was present in 3 patients. It is a relatively frequent complication of amoebic granuloma (Radke, 1955). It may occur around a colostomy or a fistula, or involve the perianal skin, or there may be no direct contact with amoebic lesions elsewhere (Song, 1956). In the third type the amoebae may be introduced into the damaged skin by contaminated fingers (Engman and Heithaus, 1919), or may spread to the skin from the blood stream; two forms were observed: continuous spreading ulceration or small circumscribed lesions.

Cerebral abscess in patients with amoebiasis is not always of proven amoebic origin (Kean *et alii*). The earlier literature was reviewed by Armitage (1919) and a further case recorded. The complication is nearly always fatal, and its course closely resembles that of pyogenic cerebral abscess. It is difficult to distinguish amoebae from large macrophages in the damaged brain tissue.

SUMMARY

Forty-four cases of amoebiasis have presented at the Melbourne teaching hospitals between 1935 and 1958.

A high mortality and high incidence of complications were noted. This is clearly related to difficulties experienced in diagnosis.

It is suggested that in the absence of distinctive clinical features, an awareness of the condition and perseverance in the face of negative examinations are necessary if the diagnosis is to be established in the early stages of the illness.

ACKNOWLEDGEMENTS

We are indebted to the Honorary Medical Staffs of the Melbourne teaching hospitals for access to case histories and for permission to publish the series included in this paper.

REFERENCES

ARMITAGE, F. L. (1919), *J. trop. Med. Hyg.*, vol. 22, page 69.

BALDWIN, A. H., HEYDON, G. M., and BROBEN, J. A. (1927), *Med. J. Aust.*, vol. 1, page 374.

BEARUP, A. J., LAWRENCE, J. J., and HEYDON, G. A. M. (1949), *Med. J. Aust.*, vol. 2, page 7.

COLVILLE, H. C. (1922), *Med. J. Aust.*, vol. 1, page 96.

CORLETTE, C. E. (1915), *Med. J. Aust.*, vol. 1, page 427.

COWLING, D. C., and PLUNKETT, P. (1958), personal communication.

DAVIES, J. A. L. (1955), *Proc. roy. Soc. Med.*, vol. 48, page 491.

DEW, H. R. (1921), *Med. J. Aust.*, vol. 2, page 510.

ENGMAN, M. F., and HEITHAUS, A. S. (1919), *J. cutan. Dis.*, vol. 37, page 715.

FIASCHI, T. (1898), *Aust. Med. Gazette*, vol. 17, page 511.

GOLDSMITH, T. (1902), *Trans. Intercolon. Med. Cong. Aust.*, 6th Session, page 180.

HALL, B., and CARRUTHERS, H. L. (1957), *Med. J. Aust.*, vol. 1, page 32.

ISBISTER, J. L. T. (1898), *Aust. Med. Gazette*, vol. 17, page 512.

—— (1899), *Trans. Intercolon. Med. Cong. Aust.*, 5th Session, page 82.

KEAN, B. H. (1955), *Arch. intern. Med.*, vol. 96, page 667.

——, GILMORE, H. R., and VAN STONE, W. W. (1956), *Ann. intern. Med.*, vol. 44, page 831.

LAMONT, N. McE., and POOLER, N. R. (1958), *Quart. J. Med.*, vol. 27, page 389.

LANCASTER, H. O. (1953), *Med. J. Aust.*, vol. 1, page 552.

MAEGRAITH, B., and HARINASUTA, C. (1953), *Trans. roy. Soc. trop. Med. Hyg.*, vol. 47, page 582.

MAPLESTONE, P. A. (1921), *Ann. trop. Med. Parasit.*, vol. 14, page 283.

NELSON, W. H., and SHEARMAN, C. H. (1918), *Med. J. Aust.*, vol. 1, page 44.

O'BRIEN, D. P. (1899), *Aust. Med. Gazette*, vol. 18, page 390.

OCHSNER, A., and DEBAKEY, M. (1943), *Surgery*, vol. 13, pages 460, 612.

PATTERSON, S. W. (1923), *Med. J. Aust.*, vol. 1, page 323.

RADKE, R. A. (1953), *Gastroenterology*, vol. 25, page 1.

—— (1955), *Ann. intern. Med.*, vol. 43, page 1048.

RIVES, J. D., HEIBNER, W. C., and POWELL, J. L. (1955), *Surg. Clin. N. Amer.*, vol. 35, page 1421.

SHAW, H. M., and HUGHES, E. S. R. (1951), *Aust. N.Z. J. Surg.*, vol. 21, page 312.

SODEMAN, W. A. (1952), *Med. Clin. N. Amer.*, vol. 36, page 405.

SONG, Y. S. (1956), *Ann. intern. Med.*, vol. 44, page 1211.

VERCO, J. C. (1899), *Aust. Med. Gazette*, vol. 18, page 66.

WILLIS, H. H. (1923), *Med. J. Aust.*, vol. 2, page 682.

GUN FOR THE ATTACHMENT OF CLIPS TO SMALL VESSELS IN DEEP PELVIC SURGERY

By D. Fairbanks and A. S. Manson

Physics Department, Peter MacCallum Clinic

and Graham Godfrey

Department of Obstetrics and Gynaecology, University of Melbourne

In certain pelvic dissections, such as those entailed in radical hysterectomy and the pelvic exenterations, difficulty may be experienced in applying ligatures to deeply placed vessels which cannot be controlled by diathermy. This applies particularly to veins, which exhibit increased friability in arteriosclerotic subjects and in those who have had previous pelvic irradiation.

Often it is difficult to engage a free tie around the point of a vertically disposed clamp, whilst suture ligatures carry the risk of wounding other vessels. Moreover, running a knot down considerable depth requires a degree of tension which is apt to cut through a friable vessel.

In relatively superficial areas it is not difficult to apply metal clips with short hand forceps, but it has been found to be almost impossible to carry this out satisfactorily with long forceps in deep situations. This is because the clip must be held firmly enough to avoid displacement and at the same time must not be prematurely compressed. Furthermore, the mechanical disadvantage imposed by long forceps impedes firm clamping of the clip.

For these reasons the Physics Department of the Peter MacCallum Clinic was asked to design and make an instrument capable of securely applying metal clips at depth.

After preliminary investigation it was found that annealed fine silver clips were suitable

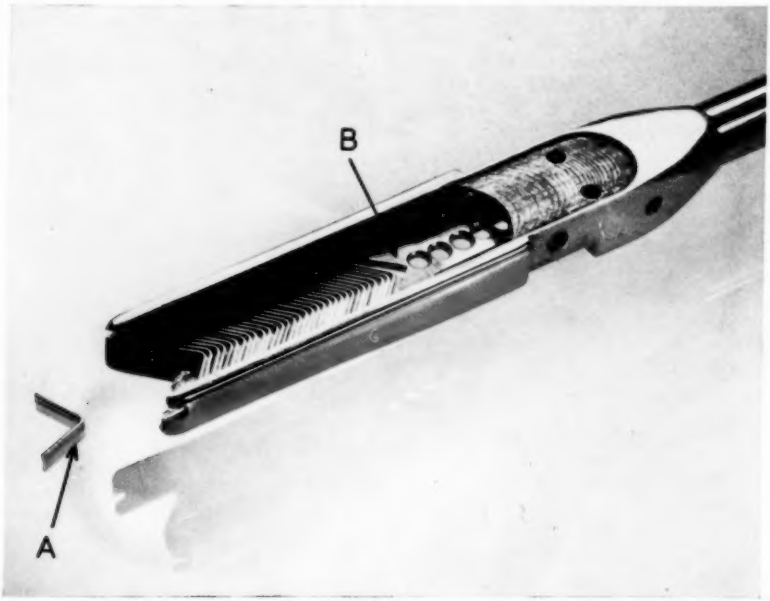


FIG. I. Photo shows a single clip "A" and a number of clips in the magazine with the spring loaded pusher "B" behind them.

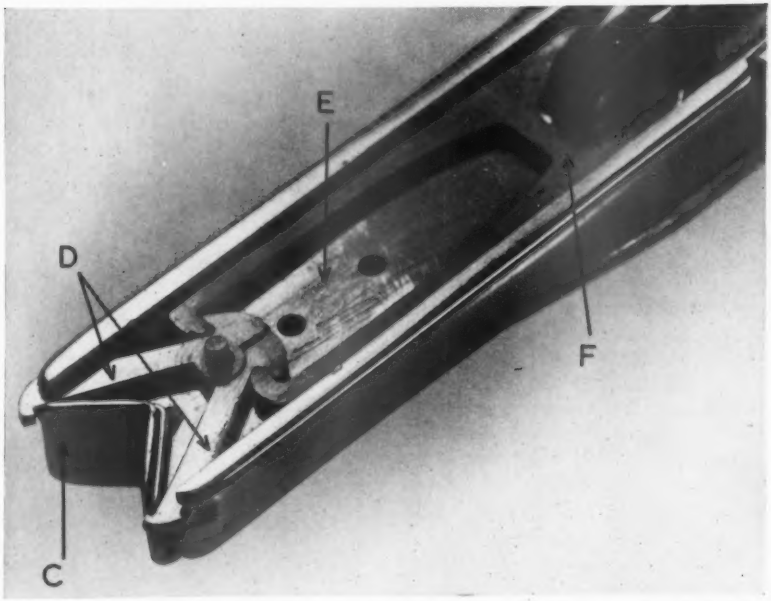


FIG. II. Selector arm "C" loads clips singly into position between the jaws which grip the clip. Also shown are "E," the magazine cover plate; "D," the jaws, and "F" the jaw operating plate which opens and closes the jaws as it is driven back and forward.

FIG. III. The selector arm has now retracted to its initial position, leaving the clip held lightly but firmly within the jaws which then close upon it as in Fig. V.
This action has all been accomplished on the pull of the trigger, which on release is returned to its orginal position and causes the jaws to open and release the clip.

for the purpose, and an automatic applicator with a magazine holding 40 of these clips was then designed and made.

The instrument is sterilized by autoclaving, and cleaned after use by immersion in hydrogen peroxide solution, followed by thorough rinsing in water. This seems to be the best way to remove traces of blood. Liquid paraffin is used for lubrication.

It is important to avoid tentative pulling on the trigger, as this may cause a clip to jam the mechanism. The trigger must be pulled evenly and to the full range with a steady squeezing action. When loading the magazine each clip should be inspected and any faulty clip must be discarded. All clips must have the standard angle of 90°.

Clips may be placed behind a clamp or directly on a vessel. The instrument can at times also be used to pinch off a retracted vessel on the side wall of the pelvis. This is because the small compressing jaws lie close to the left side of the distal end of the applicator, so that lateral pressure with the tip causes soft tissues to bulge within the area of their grasp. Since the instrument can be used with equal facility by either hand this action is applicable on either side of the pelvis.

The gun has now been in practical use in upwards of a dozen cases. So far it has not been used freely for the purpose of saving time, but has been restricted to dealing with vessels where there is difficulty in applying ligatures and diathermy is ineffective or unsuitable. It cannot be used in narrow crevices, but such situations are usually amenable to packing. Nor is it designed to cope with vessels of greater diameter than approximately 3-4 mm. Despite these limitations it has repeatedly proved to be most valuable in use. It is particularly satisfying when by simply squeezing a trigger one immediately controls an awkwardly placed bleeding vessel under circumstances where experience suggests that there is a high probability that attempts at placing ligatures may cause tearing of vessels and a series of haemorrhages of increasing magnitude, each becoming more difficult to control.

DESCRIPTION OF INSTRUMENT

The instrument described seals the vessels by attaching clips of 0.02 in. x 0.05 in. annealed fine silver wire. These clips, which can be seen in Fig. I, have arms 5/16 in. long, set at 90°. It will be noted that the junction of the two arms is in the form of a radius, an important factor in ensuring that the clip, when squeezed on the vessel, does not spring open again.

The gun comprises three separate, but interrelated, systems. A magazine holding a bank of 40 clips consists of a simple channel with a spring loaded pusher feeding the clips forward. The magazine is clearly seen in Fig. I, and in the appropriate view of Fig. VII. The second part of the system, the jaw mechanism, closes the clips on the vessel. This operation can be seen in Figs. II, III and IV and the actuation of the jaw system by the lever and push rod arrangement from Figs. III, IV and V. Thirdly, comes the selector arm (Part C, Fig. VI) which selects a clip from the magazine, feeds it to the jaws and then returns to its initial position at which time the next clip is pushed into the recess on the selector arm. The selector arm is operated by the cam bar shown as G in the exploded view (Fig. V) and in Fig. VII. The cam bar is made to move sideways and carry the tang of the selector arm with it as a result of the action of the vertical projection from the back of the trigger which rides in the slot H, when the trigger and its carriage is drawn back. It will be noted that the trigger is free to pivot about the screw (I) on its carriage so that when the trigger is pulled it first raises the vertical projection to engage in the slot, the vertical projection then travelling back with the trigger and causing the shaped slot in the cam bar to act as an elongated cam and drive the bar sideways. On the release of the trigger it is necessary to avoid the actions described from being operated in reverse and this is achieved because the trigger, again pivotting about (I), first allows the vertical projection to drop and disengage from the slot. This non-reversal of the action is essential otherwise clips would be loaded on both the forward and return strokes of the trigger causing jamming of the mechanism. The disengagement is therefore made positive by a small addition to the under-side of the cam bar at the point where cam action takes place. The entire gun, views of both sides

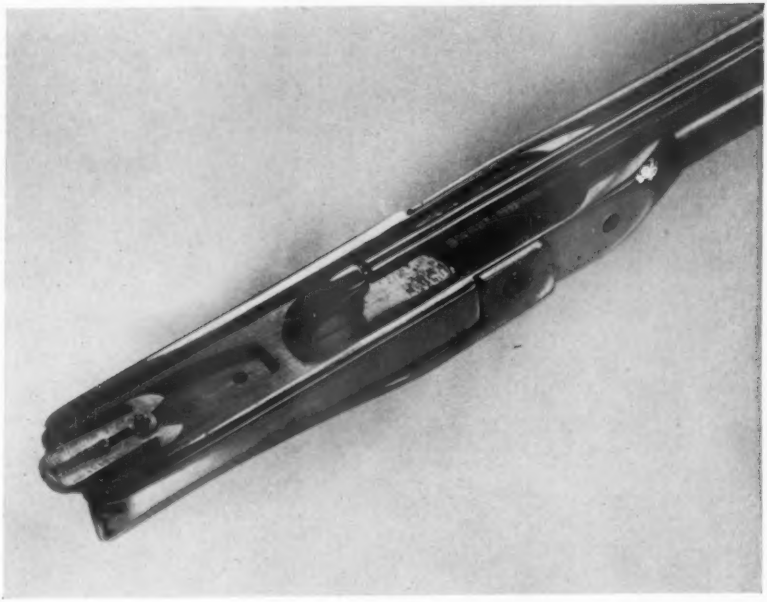


FIG. IV.

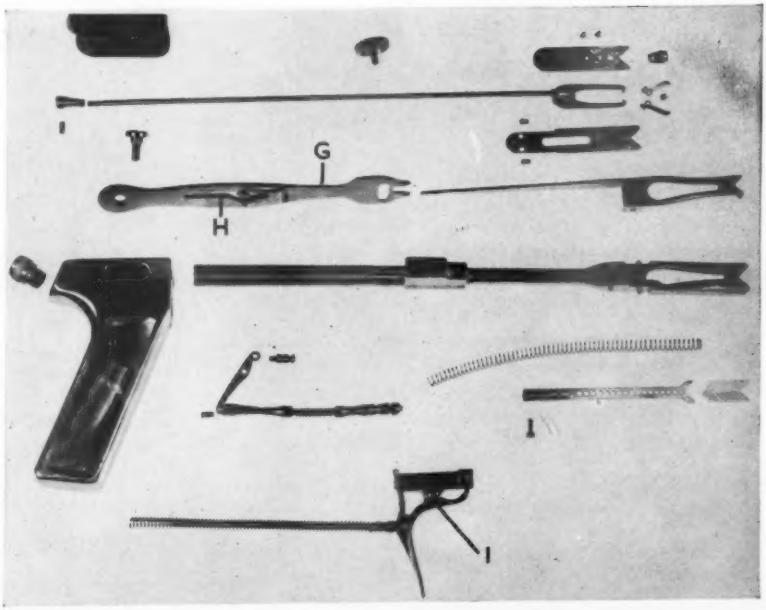


FIG. V. "Exploded" view of gun showing components in its construction.

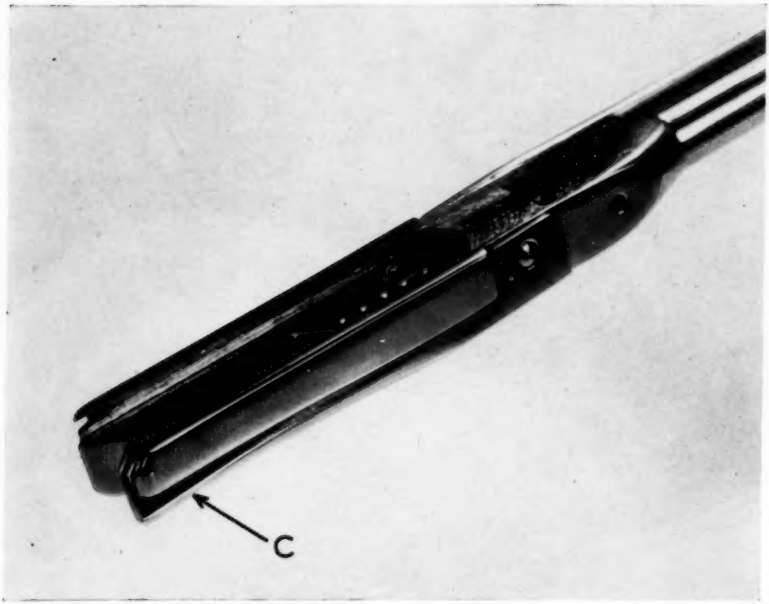


FIG. VI. Selector arm "C" is shown in position retaining bank of clips in magazine against pressure of pusher.

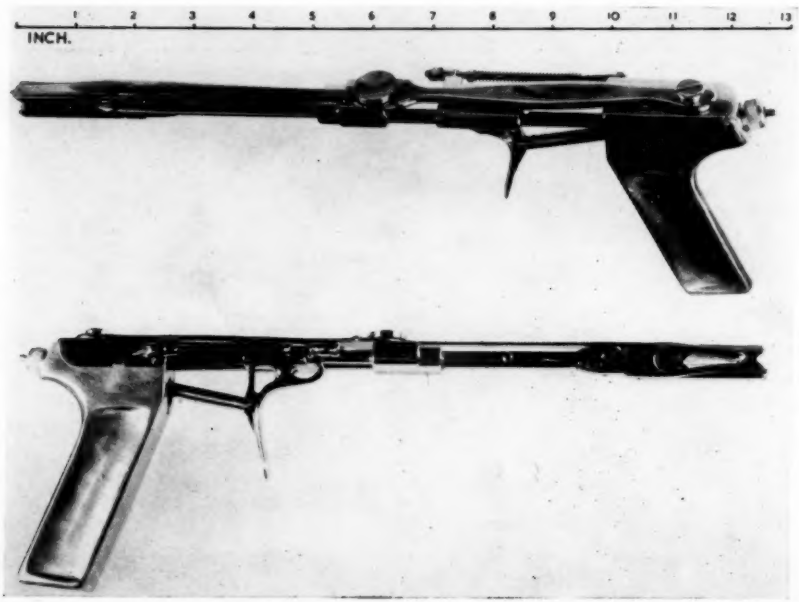


FIG. VII. Complete gun, showing aperture for loading clips, clips in place and pusher "B."

of which are shown in Fig. VII, weighs 19¼ ozs. It is fabricated from appropriate non-corrosive material and the whole can be sterilized.

SUMMARY

The paper describes a gun suitable for the attachment of clips to small vessels in the course of deep pelvic surgery. It is particularly useful where difficulty is experienced in applying ligatures.

ACKNOWLEDGEMENTS

The authors are indebted to Mr. L. Benson, of J. W. Handley Pty. Ltd., for the supply and rolling of fine silver wire; to Mr. H. A. Taylor, of H. A. Taylor and Sons Pty. Ltd., for the use of equipment during the early developmental stages; and to Mr. F. N. Ashburner, of Greer and Ashburner Pty. Ltd., for the design and manufacture of experimental clips, and for production of the clips finally used.

INTACT EXTRUSION OF HYDATID CYSTS

By W. W. Woodward

Launceston

THE fragility of the germinal and laminated membranes of the hydatid cyst is notorious. Nevertheless intact extrusion has been observed. In this event the fluid and scolices remain unspilled while the cyst performs a remarkable escape. It makes its way through a rent in the host's fibrous adventitial membrane and remains intact as it does so. Hydatid cysts burst so readily that it would be difficult to believe this precarious passage possible without rupture had it not been observed.

In the English language intact extrusion has been described by Dew (1928) who gave foreign references and an illustration showing this phenomenon at necropsy. Another photograph taken at a necropsy and further foreign references are given by Hueston (1952).

In the present paper there follow notes on further examples, including one where there was also intact transperitoneal migration of a liver cyst to the bottom of the peritoneal cavity, that is into the recto-vesical pouch. This, too, has been previously described; the late Sir Alexander MacCormick of Sydney met in the pelvis such a cyst containing two pints of fluid, while Dévé designated the condition of transfer of a mature cyst to a new site as "L'hydatique primitive hétérotopique des séreuses" (Dew). This phenomenon is distinct from and less common than secondary echinococcosis which results from rupture of all membranes of a cyst, as was first proposed in the last year of his life, 1793, by John Hunter (Dévé, 1919). Secondary pelvic cysts are common, but Dévé in 1924 could find only 12 cases in the literature which appeared to be primary in the pelvis (Dew, 1928).

The writer, in a limited survey of the literature, has not been able to find a description of intact removal of such a wandering, primary, cyst from the recto-vesical pouch. It so happens that on Sir Harold Dew's advice this came to be done for a patient to be described and the object of the present communication is to show the value of early operation when intact extrusion is a possibility. In considering the surgical management it is of value to distinguish partial from total intact extrusions.

Partial Intact Extrusions

Downward

(i) Mr. P. Braithwaite of Hobart met an example of partial intact extrusion which was responsible for an unusual clinical story.

In a girl aged fourteen years, an inmate of a mental hospital, there had been noted a rapid enlargement in the size of an hemispherical epigastric mass. Indeed it had doubled its size over a period of only twenty-four hours. This, of course, was a remarkable rate of expansion for any epigastric mass, but at laparotomy an hydatid cyst, still intact, was found to have broken free from an adventitial sac in the liver. It was removed and recovery followed.

(ii) Mr. T. W. Horne observed partial extrusion of an intact hydatid from the liver of a seven year old boy admitted to the Royal Hobart Hospital.

On 19 Sept. 1954 Peter M. fell into a trench, striking his abdomen on the edge of the trench as he fell. After the fall he became "off colour." On admission four days later he was vomiting and his abdomen was obviously distended.

Laparotomy revealed an hydatid of the usual appearance in the left lobe of the liver but this alone would not have accounted for the symptoms. On the inferior surface of the liver there was another hydatid of about the same size, 6 or 7 cms. in diameter. This cyst was partially extruded through a rent in the liver's adventitial membrane. The parasite's own membranes were intact. Time was allowed for the extrusion to complete itself and then this cyst was delivered out of the abdomen unbroken. Mr. Horne dealt in the conventional manner with the remaining cyst. Recovery was uneventful.

Upward

In the example of partial extrusion now to be described the cyst had again remained intact. Thoracotomy was done before rupture occurred.

Case report

L.A.M., aged thirty-one, was referred to the writer on 22 Oct. 1955 by Dr. J. Hunn of Wynyard. The patient had a two-year history of 4 attacks of right-sided pleuritic-like pain. Pleuritic pain was reported

in a somewhat similar case by McConchie (1958). Dr. Hunn treated the fourth attack. He noted that pyrexia was slight, 99.0° F., and that there was no friction rub. He withheld any form of chemotherapy and the patient's pain subsided within thirty-six hours. The patient had lived on a sheep farm up to the age of twenty. His Casoni test was positive. In the chest film the radiologist, Dr. R. E. Grant, reported a localized, dome-shaped elevation of the right hemidiaphragm. The tall dome was posteriorly situated and though relatively inconspicuous in the P.A. view showed prominently in the lateral view (Fig. I).

FIG. I. Hydatid from the liver of an adult elevating and stretching the diaphragm and found at right lower thoracotomy to have partially escaped from the adventitial covering provided by the liver.

On 3 Nov. 1955 at St. Vincent's Hospital, Launceston, under general anaesthesia by Dr. H. J. C. Engisch, a right lower thoracotomy was performed.

Thoracotomy confirmed that the dome was the upper half of an intact hydatid. The whole cyst had the shape of an hour-glass. Over the upper pole there were some attenuated fibres belonging to the central tendon of the diaphragm. The cyst could be seen in spaces between these fibres. These were then divided by scissors and the cyst was observed to emerge intact through the already existing rent in the hepatic adventitia. After about twenty minutes the whole cyst gained the pleural cavity. From here it was lifted out by hand, still unbroken. The adventitial sac in the liver was then seen to contain three other hydatid cysts. By comparison with the partially extruded cyst these were very small, the largest being of not more than 1.5 cm. in diameter. These were easily removed intact in a spoon. The adventitial sac in the liver was then washed with formalin, the diaphragm was repaired and the chest wall closed with water-seal drainage. Recovery was uneventful.

In this instance the original adventitia in the upper part of the liver had been penetrated by the cyst, while the overlying tendinous part of the diaphragm had been elevated and stretched to the point where its fibres had become separated. It seems possible that these splits had caused the attacks of pleuritic-like pain.

Dome-shaped diaphragmatic elevations are not of course all due to hydatid disease. Indeed, some, less elevated than the present, are not due to any disease and merely represent diaphragmatic deformations of the liver (Christie, 1951). In this patient, however, thoracotomy gained the advantage of intact removal of the partially extruded cyst, thus forestalling the complications likely to follow rupture.

TOTAL INTACT EXTRUSIONS

Mr. S. C. Fitzpatrick, of Hamilton, Victoria, told the writer that Mr. Balcombe Quick, of Melbourne, knew of a total intact extrusion, and Mr. Quick confirms that this occurred in Echuca many years ago. From memory he wrote that a laparotomy was done for haemorrhage of undetermined origin. Operation revealed "quite a large hydatid cyst free and unruptured, with bleeding from the liver bed" (Quick, 1957). Recently another intact extrusion from the liver, also accompanied by intraperitoneal bleeding, has been described by Webb (1958). In that instance the cyst measured 17.5 x 12.5 x 10 cms. and its escape from the liver caused severe shock. At laparotomy Mr. Webb allowed the patient's respiratory movements to expel this large cyst and recovery followed.

Professor Stammers, of Birmingham, told the writer of an example of intact total extrusion into the pleural cavity. This phenomenon was discussed at a meeting in Cardiff in 1943 by Professor A. W. Sheen. There was total intact extrusion from the lung, and the cyst was found still intact in the bottom of the pleural cavity on the same side.

TOTAL EXTRUSION WITH INTACT TRANS-PERITONEAL MIGRATION

In the example to be described below, a solitary hepatic cyst broke through its adventitial covering in the liver. It must then have moved across the face of the great omentum, for at operation it was found in the recto-vesical pouch, from the bottom of which it was delivered still unbroken.

Case report

A boy whose past medical history consisted of sinusitis, tonsillectomy and two months' abdominal pain, was referred by Mr. D. A. T. Farrar to the present writer because of a smooth round swelling in the midline of the epigastrium. The swelling was half-way between the umbilicus and the xiphisternum. Its diameter was about 6 cms., and it was noted to be very mobile.

Stephen T.'s age was ten years and his weight 3 stone 13 pounds (25 Kg).

The immediate and the delayed Casoni intradermal test and the hydatid complement fixation test by both warm and ice-box methods were all negative. There were 15.8 grams per cent. of haemoglobin and 13,000 white blood cells per cmm. Of these 1 per cent. were eosinophil but a raised percentage of eosinophil cells is not expected in hydatid disease (Ramsay, 1906) unless there has been recent release of hydatid antigen as by rupture of the cyst or surgery (Waddle, 1950). A provisional diagnosis of hydatid disease was greatly assisted by the radiologic demonstration of another lesion, a chest film showing a spherical homogeneous opacity which the lateral view localized in the anterior segment of the right upper lobe. This appearance in the southern parts of Australia is commonly due to hydatid. The diameter of this shadow was a little less than that of a penny, i.e. less than 3.0 cms.

Vigorous games were banned for the interim and admission to hospital for laparotomy arranged for ten days hence, but this was not soon enough; for nine days later at 11 a.m. the boy felt an epigastric pain which soon grew in severity. It was not a colic, and fortunately, as it turned out, he felt that he had to lie still. His mother said that he called out:—"Mum, feel my tummy. That lump's gone." She brought him into the city from the bush and on abdominal examination in the evening there was generalized guarding with tenderness maximal in the epigastrium.

The writer now mistakenly assumed that the hepatic hydatid had burst and pictured for the boy a future of multiple abdominal hydatids with all their sequelae: he consulted Sir Harold Dew by telephone and was advised that the laparotomy should still be done. Accordingly at the General Hospital, Launceston, on 12 Feb. 1957, under general anaesthesia by Dr. John Woodley, a midline upper abdominal incision was made. After opening the peritoneum, an adventitial sac was seen on the anterior surface of the liver. The sac was empty and no other abnormality could be found in the liver.

A peritoneal search was therefore gently begun and carried on until finally in the recto-vesical pouch the bare cyst was seen intact. Dew (1958) writes:—"Typically in young subjects we find simple and univesicular cysts . . ." and such was the case here.

About one square centimetre of outer layer of laminated membrane was seen to be missing from one pole of the cyst, and a piece of whitish material of corresponding size was found on the face of the great omentum. This small piece of parasitic tissue has been commented upon thus:—"All cysts, even healthy univesicular, may show a quiet shedding or moulting of these layers of hyaline from the outer surface. This surface is older and has a higher tension than the inner layers. Also the mild movement down the abdominal cavity could certainly peel off a little, microscopical mainly, but sometimes bigger pieces of the laminated membrane." (Dew, 1957.) There was no other abnormality discoverable in the abdomen despite a complete search.

The next step at operation was to lengthen the incision downwards. The buttocks were then elevated thus allowing the cyst to roll slowly out through the wound into a waiting kidney dish.

Especially at the weakened pole rupture was feared but fortunately the cyst did not break (Fig. II).

FIG. II. Univesicular hydatid cyst totally extruded from the anterior surface of the liver of a boy and removed at laparotomy from the recto-vesical pouch of the peritoneum.

On Sir Harold Dew's advice thoracotomy was postponed so as to reduce the risk of anaphylaxis. The significance of the time-interval between opportunities for the release of hydatid antigen is discussed in Dew's (1928) chapter on anaphylaxis and by Fitzpatrick (1951). Though the cyst had not burst, there had been opportunity, theoretically at least, for the small piece of laminated membrane found on the great omentum to act as an antigen. Moreover the lung shadow was very much smaller than a large number of lung cysts in other patients which had not spontaneously burst. On these grounds delay obviously offered more safety than early

thoracotomy. The boy was seen in April, July, September and December. In December the intradermal Casoni fluid after thirty minutes gave a wheal measuring 3.4 x 2.6 cms. This was the first positive reaction. As a chest X-ray showed no enlargement of the right upper lobe shadow, thoracotomy was further delayed. Had this shadow been enlarging or changing its shape there would probably have been more risk of rupture from delay than from handling, and the thoracotomy would in that case have been done sooner.

Thirteen months after it was first found, the lung opacity as seen in P.A. and lateral films was still spherical. During these thirteen months it had enlarged in diameter, according to a caliper measurement, by no more than one millimetre. This rate of increase in diameter, if it can be accepted as an increase, was much slower than that of four cysts recorded by Waddle (1950) (a little over one millimetre, two millimetres, three and four millimetres a month respectively), and of one recorded by Fitzpatrick (1929) where there was a fifteen millimetre increase in diameter in nineteen months. It is not known when the parasite first lodged in the boy's lung, but even if it had been present all his life, an unlikely event, then it would have averaged nearly three millimetres in each twelve months up to the time when his chest was first X-rayed. Many authors have commented on the variability of growth rates of hydatids in the lung and have also noted that any one cyst does not have a steady rate of expansion.

The hydatid complement fixation test was repeated and to both methods was still negative, but when a cyst is univesicular and unruptured a negative result to this test is often obtained, as has been noted by many writers on this subject.

Though the progression of the lung shadow was minimal it was decided now to operate and on 24th March 1958 at the same hospital under general anaesthesia by the same anaesthetist an anterior thoracotomy was performed. An uncomplicated univesicular cyst was delivered intact. The method described by Barrett and Thomas, itself an artificial intact extrusion, was used instead of the alternative technique of partial, that is almost complete, aspiration at operation followed immediately by removal of the collapsed cyst.

Ninety patients with unruptured cysts operated on by Fitzpatrick, who uses aspiration, remained free from recurrence (Fitzpatrick, 1954). The present writer frequently prefers Fitzpatrick's technique, for example when the cyst is too large or poorly situated for artificial extrusion or when gross emphysema or some general condition of the patient makes preferable a procedure less time-consuming than extrusion, one of the outstanding features of which is the necessity for the surgeon, as emphazised by Barrett and Thomas, to be prepared to wait for twenty or more minutes while the cyst comes through the incised adventitia.

DISCUSSION

While it is not uncommon for hydatid cysts to be found in the peritoneal or pleural cavities, these are usually secondary or daughter cysts resulting from the rupture of the membranes of a preceding hydatid. In short they are a manifestation of metastatic or secondary echinococcosis.

A quite different phenomenon is the extrusion intact of a primary hydatid, and if operation is done early in suspected cases intact extrusion of these may be found to be not so extremely uncommon as has been supposed.

The value of early surgery is that the relevant cavity may be cleared of the parasite at one operation before rupture of the extruded cyst. Early surgery may protect the patient from the growth of secondary cysts with, in turn, all the sequelae of their development. If at operation it is found that the cyst has already burst then the operation is still not wasted because it provides opportunity for the removal of the membranes.

If the cyst is not immediately apparent where it was to be expected then a very gentle search should be made throughout the opened serosal cavity in case it has migrated intact, for this as has been shown is a possible consequence of intact extrusion.

SUMMARY

(1) Partial extrusions of three hepatic hydatid cysts are reported from Tasmania, thus adding to the existing accounts of these events. Two were downward into the peritoneum and one upward into an expanded subphrenic space. These partial extrusions were all seen at operation.

(2) Total extrusions known to have occurred elsewhere are briefly mentioned. A Tasmanian total extrusion is described in a case report. Total extrusion from this patient's liver was followed by intact transperitoneal migration into the recto-vesical pouch. Operation happened to be done before rupture occurred and the cyst was delivered intact from the recto-vesical pouch, an operation to which the writer has not found previous reference in English, though it cannot be said that anything like an exhaustive search has been made.

(3) Because of the risk of rupture of the newly uncovered hydatid it is recommended that surgery should be resorted to as an emergency when intact extrusion is a possibility.

(4) If the cyst is not seen where it was to be expected, then a very gentle exploration of the remainder of the opened serosal cavity is indicated, in case the cyst has migrated intact.

(5) Finally, there is the possibility that intact extrusion may be found to be not so extremely uncommon a phenomenon if operation in a suspected case is done early, i.e. before rupture of the cyst.

ACKNOWLEDGEMENT

The photographs were taken by Mr. A. Markovitch, Clinical Photographer, Launceston General Hospital.

REFERENCES

BARRETT, N. R., and THOMAS, D. (1952), *Brit J. Surg.*, vol. 40, page 222.

BRAITHWAITE, P. (1947), Lecture to a Tasmanian State Meeting of the Royal Australasian College of Surgeons.

CHRISTIE, G. S. (1951), *Aust. N.Z. J. Surg.*, vol. 20, page 289.

DEVE, F. (1919), *Lancet*, vol. 2, page 835.

DEW, H. R. (1928), "Hydatid Disease. Its Pathology Diagnosis and Treatment", Sydney, Australasian Medical Publishing Co.

—— (1957), Personal communication.

—— (1958), *Brit. J. Surg.*, vol. 45, page 447.

FITZPATRICK, S. C. (1929), *Med. J. Aust.*, vol. 2, page 214.

—— (1951), *Aust. N.Z. J. Surg.*, vol. 20, page 278.

—— (1954), *Aust N.Z. J. Surg.*, vol. 24, page 109.

—— (1957), Personal communication.

HORNE, T. W. (1957), Personal communication.

HUESTON, J. T. (1952), *Aust. N.Z. J. Surg.*, vol. 22, page 149.

MCCONCHIE, I. (1958), *Aust. N.Z. J. Surg.*, vol. 27, page 204.

QUICK, B. (1957), Personal communication.

RAMSAY, J. (1906), *Intercolonial Med. J. Aust.*, vol. 11, page 380.

STAMMERS, F. A. R. (1958), Personal communication.

WADDLE, N. (1950), *Aust. N.Z. J. Surg.*, vol. 19, page 273.

WEBB, R. (1958), *Aust. N.Z. J. Surg.*, vol. 28, page 71.

AN EXPERIMENTAL METHOD FOR THE PRODUCTION OF MITRAL INCOMPETENCE*

By THOMAS S. REEVE AND IAN MONK

From the Unit of Clinical Investigation, The Royal North Shore Hospital, Sydney

INTRODUCTION

SURGICAL correction of mitral incompetence has been attempted and although Davila and his associates (1955), and Lillehei (1957) and his co-workers have reported some measure of success, a standard surgical approach to this disease has not yet been established. To explore curative techniques and for haemodynamic studies it is desirable to have a suitable animal preparation for experimental purposes. Such a preparation must be capable of survival for more than one month, and must show evidence of continued mitral incompetence during this period.

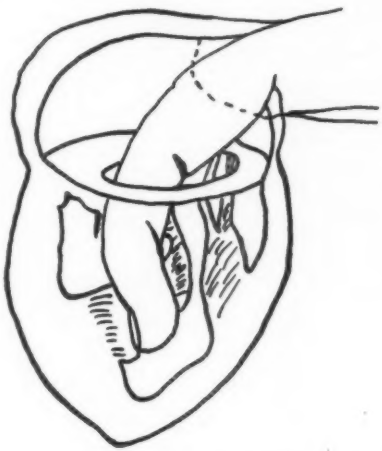


FIG. I. Finger rupture of musculus pectinatus.

Experimental animal studies of the haemodynamics have been reported by MacCallum (1906), Wiggers (1922), Barry (1927), McDowall (1927), and Shaw (1943). In most cases these studies have been made on acute preparations, but observations on animals surviving a month or more have been recorded by Haller (1955) and Morais (1957).

Subsequent studies on survivors present difficulties. Small defects produced in the mitral valve have often healed spontaneously. Furthermore, even after the successful production of incompetence there have been dense pericardial adhesions, as the pericardial envelope was transgressed at the initial procedure. This has made attempts to correct the incompetence difficult, the coronary vessels frequently being damaged during the necessary mobilization of the pericardium.

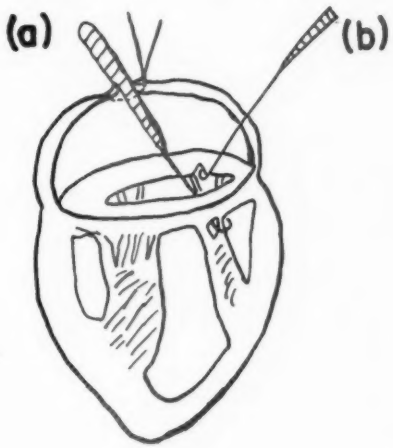


FIG. II.

This communication describes a safe, simple technique for the experimental production of mitral incompetence in sheep; a satisfactory degree of incompetence may be produced without opening the pericardial envelope. The results achieved using this method (Method 3) are compared with those achieved using two other methods (Methods 1 and 2) developed earlier, and subsequently discarded.

* This work is proceeding with the help of a Grant-in-Aid from the Life Insurance Medical Research Fund of Australia and New Zealand.

MATERIAL AND METHODS

Sheep (two-toothed ewes) of varying breeds, averaging 25-30 Kg. weight, were anaesthetized with intravenous pentobarbitone, 25 mg/Kg. of body weight. The animals were ventilated with 100 per cent. oxygen throughout the procedure, oxygenation being maintained by means of a Palmer pump connected to a soda-lime canister and cuffed endotracheal Magill's tube. The animals were starved for thirty-six hours prior to operation to prevent ruminal distension under anaesthesia. The left hemithorax was approached through the fifth intercostal space. All sheep were given 0.5 mgm. digoxin and 2 cc. Mersalyl intramuscularly daily for three days after operation.

All surviving animals in which a mitral systolic murmur has been noted several weeks after operation have been submitted to right heart catheterization in order to measure the pulmonary capillary venous pressure.

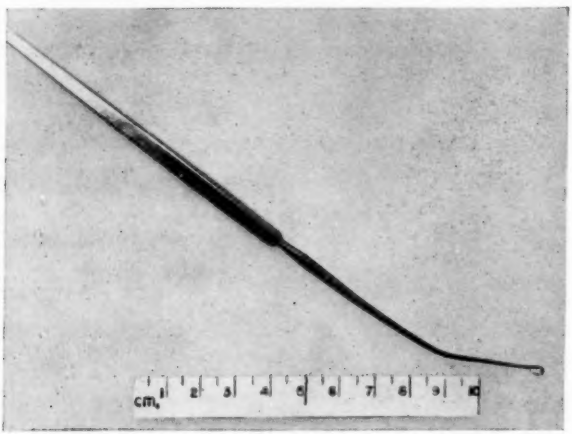
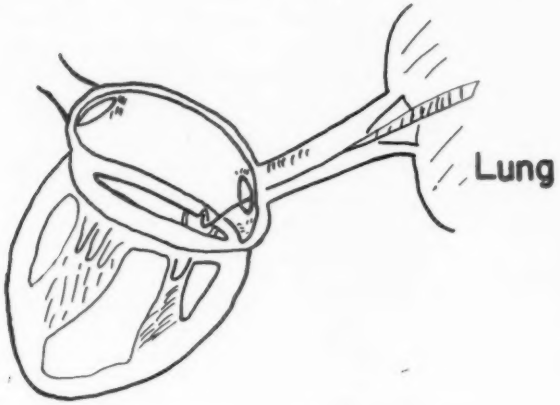


FIG. III. The modified Gillies hook used for tearing the posterior cusp of the mitral valve.

TABLE 1

Method	*Number of Sheep Used*	*Survivors* and degree of Incompetence*	*Deaths and Cause*
1	12	2	Operative haemorrhage 1
		+++, 2	Acute post-operative pulmonary oedema within 24 hours 6
			Post-operative haemorrhage 2
			Empyema—7 days 1
			10
2	6	4	Intractable ventricular fibrillation during operation 1
		O, 1	Acute pulmonary oedema 4 days afterwards 1
		++ , 1	2
		+++, 2	
3	38	27	Unsuspected perforation of left ventricle cardiac tamponade 1
		O, 1	Post-operative haemorrhage 1
		+, 3	Acute pulmonary oedema 24 hours post-operatively 3
		++, 12	" " " 2 days " " 2
		+++, 7	" " " 5 " " " 1
		++++, 4	" " " 9 " " " 1
			Empyema 12 days post-operatively 1
			Endocarditis 28 days post-operatively 1
			11

*Animals were accepted as survivors if they lived for thirty days, or until an earlier operative procedure is carried out.



SHEEP 30. MITRAL INCOMPETENCE

P.C.V.P. = 16/7, mean = 11 P.C.V.P. → P.A. P.A. = 30/15, mean=19

P.A. R.V. = 36/5 R.A. = 10/6

SHEEP NO. 28 MITRAL INCOMPETENCE

P.C.V.P. = 44/40, Mean = 39 P.A. = 78/46

P.A. R.V. = 78/18 R.A. =20/-4 S.V.C.=10/4

FIGS. V and VI. Records of right heart catheterization in two animals prepared by Method 3, the pulmonary capillary venous pressure is raised in both animals.

Method 1

The pericardium was incised parallel to the phrenic nerve. A purse string suture of 00 atraumatic silk was placed in the left atrial appendage. The atrial wall was opened within the suture, and the right index finger was inserted into the left ventricle. One or two chordae tendineae were picked up by the tip of the finger (Fig. 1) and torn. The finger was then withdrawn and the purse string suture was tied to secure haemostasis. A good regurgitant jet always followed.

Method 2

The procedure was identical with Method 1 to the stage of opening the atrial wall, a Gillies nerve hook was inserted into the left atrium instead of the finger and the hook was pulled gently against the posterior cusp of the mitral valve, or a chorda tendinea. It was then given a sharp tug (Fig. II) and withdrawn; a good regurgitant jet was usually produced.

Method 3

When the chest was opened, the left lung was retracted well laterally, exposing the left superior pulmonary vein. This was gently dissected from the investing pleura, and a heavy linen thread was passed behind the vein and held firmly in the operator's left hand putting the vein under moderate tension. A Gillies hook modified for the purpose (Fig. III) was then inserted through the wall of the pulmonary vein into its lumen. It was then advanced towards the ventricle. When its tip was judged to have entered the ventricle it was gently withdrawn along the posterior wall until its progress was impeded by the posterior cusp of the mitral valve. At this stage a sharp tug (Fig. IV) was given, and the hook was drawn into the atrial appendage. Successful production of incompetence was marked by a sudden increase in size of the atrium and the presence of a palpable thrill at the level of the atrioventricular ring. If the effect was judged to be too slight, the manoeuvre was repeated. The hook was then withdrawn and the opening in the pulmonary vein was repaired with 00000 atraumatic silk. This manoeuvre leaves the pulmonary vein patent, and the pericardium free from adhesions.

RESULTS

These are shown in Table I. In animals operated upon by Method I the mortality was so high as to be prohibitive. Moreover, our purpose was to explore methods for the correction of mitral incompetence as reported by Monk *et alii* (1958) and the few sheep surviving were unable to withstand reparative surgery. Animals operated upon by Method 2 lived longer but had pericardial adhesions which hampered subsequent efforts at surgical correction of their mitral incompetence.

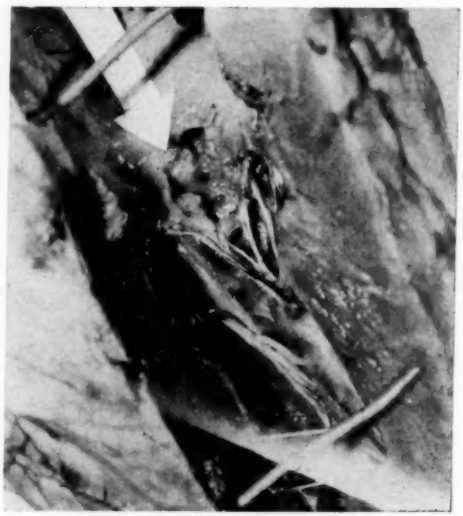


FIG. VII. The arrow points to a typical defect produced by Method 3 in the posterior cusp of the mitral valve of sheep.

Method 3 has provided a good supply of animals for corrective studies. The pulmonary capillary venous pressure (Figs. V and VI) has not been raised in all instances but at re-exploration almost every animal has had a palpable regurgitant jet and an enlarged left atrium. An autopsy, evidence of a mitral valve lesion has been present in all animals (Fig. VII). Furthermore there have been no pericardial adhesions.

Animals have been subjected to right heart catheterization two to four weeks after they have been rendered incompetent. It has been noted that those animals with severe incompetence develop pulmonary oedema after catheterization. Digoxin and Mersalyl help some but many such animals die.

Left ventricular angiography has also been used in the study of the haemodynamics of mitral incompetence. This often produces death in animals with a high degree of incompetence.

SUMMARY

1. A new method is described for producing mitral incompetence in sheep. It provides a high percentage of survivors for long-term experiments.

2. The pericardial envelope is not opened during the procedure, and no intrapericardial adhesions are produced. This allows easy access to cardiac structures when surgical correction is attempted subsequently.

ACKNOWLEDGEMENTS

The authors are indebted to Dr. F. F. Rundle, Head of the Unit of Clinical Investigation, and Dr. I. D. Thomas for their advice and helpful criticism in the preparation of this paper.

REFERENCES

BARRY, D. T. (1927), *Arch. intern. Med.*, vol. 40, page 446.

DAVILA, J. C., GLOVER, R. P., TROUT, R. G., MANSURE, F. S., WOOD, N. E., JANTON, O. H., and IAIA, B. O. (1955), *J. thorac. Surg.*, vol. 30, page 531.

HALLER, J.. and MORROW, A. G. (1955), *Ann. Surg.*, vol. 142, page 37.

LILLEHEI, C. W., GOTT, V. C., DE WALL, R. A., and VARCO, R. L. (1957), *J.-Lancet*, vol. 77, page 446.

MACCALLUM, W. G., and MCLURE, R. D. (1906), *Johns Hopk. Hosp. Bull.*, vol. 17, page 250.

MCDOWALL, R. J. S. (1927), *Quart. J. exp. Physiol.*, vol. 16, page 1.

MONK, I., REEVE, T. S., KALOKERINOS, J., and WINGFIELD, J. (1958), *Brit. J. Surg.*, vol. 46, page 75.

MORAIS, O. J., RICHART, T. S., FRITZ, J., ACNEC, P. W., DAVILA, J. C., and GLOVER, R. P. (1957), *Ann. Surg.*, vol. 145, page 500.

SHAW, M. M., ADAMS, W. E., RASMUSSEN, R. D., HRDINA, G. S., and ARONSON, H. G. (1943), *J. thorac. Surg.*, vol. 12, page 322.

WIGGERS, C. J., and FEIL, H. (1922), *Heart*, vol. 9, page 149.

PILONIDAL SINUS OF THE AXILLA

By E. S. J. King

Department of Pathology, University of Melbourne

THE term "pilonidal sinus" has been applied most commonly to the condition found in the sacro-coccygeal region but the relatively uncommon and, in some cases, rare lesions found in other parts of the body, because of their bearing on the pathogenesis of the condition in general, have an importance and significance out of all proportion to their frequency. They incidentally emphasize that the name "pilonidal" means merely a "nest of hair" and has no topographical or aetiological connotation.

Historical Note

It is well known that the condition in the sacro-coccygeal region was recognized in the last century and that precise and accurate descriptions were then given. It is noteworthy that the modern views on the mode of their development were considered by the early writers. Despite the availability of this information, for about three-quarters of a century the suggestions and, indeed, the observations of Warren (1854) and Hodges (1880) were overlooked. This is interesting nowadays when the impact of fundamental studies compels attention, since the reason for the oversight seems to have been the failure of clinicians to keep abreast of advances in the basic sciences.

Until the beginning of the nineteenth century the accepted hypothesis of development of the body was that of "preformation". Every tissue was considered to be preformed in the embryo or even in the ovum (or spermatozoon). It followed from this that pathological conditions should be explained on the basis of their having existed since birth and changes occurring in them being due mainly to the circumstance that the tissues were abnormal to begin with.

This hypothesis had been attacked for centuries, but it was clearly moribund by the end of the eighteenth century and about 150 years ago it succumbed; it had gradually been replaced by the theory of "epigenesis". This proposed that tissues and organs, instead of being preformed, were developed by the growth of preceding cells or tissues. It was thus possible that, if circumstances were sufficiently divergent, an organ might grow differently from its normal course and this would account for variations in structure. This idea was first developed from analysis of gross changes in the foetus and adult body; it was placed on a more satisfactory footing with the introduction of histological studies and has been unequivocably established by twentieth century experimental work. Although preformation had not been seriously discussed by embryologists since the 1800s (except for echoes in the three germ layer hypothesis) its influence on pathological and clinical thought had been so profound that it continued to be the accepted principle, at least by inference, until recent times.

A condition such as pilonidal sinus was to be explained as a developmental anomaly, such a view being apparently supported by the occurrence in the postanal region of similar states indubitably congenital in time of occurrence.

Only in the last decade was the developmental hypothesis questioned by Patey and Scarff (1946, 1948) and the writer (King, 1947). This alternative view that the lesion is an acquired one is supported by the discovery of sinuses of this type in various parts of the body. These have been found in diverse places which, however, all have the common features of mobile tissue where movement causes opening and closing of a cleft or sulcus with consequent changes in pressure in its depths. Despite some disagreement regarding the precise mode of formation, opinion has come round gradually to the idea of the post-natal and acquired nature of the sinus.

Some General Features of Pilonidal Sinus

Before discussing one special and uncommon type of sinus, some characteristics common to the group are worthy of note.

Distribution

Although until recently cases had been observed only in the natal cleft, other sites have been described in the last decade. The literature suggests that some chronic sinuses, of uncertain etiology, may have been of this kind. Still other sites of pilonidal sinus, therefore, will be described.

FIG. I. Low power photomicrograph of a section showing the epithelium-lined sinus and the granuloma in the subcutaneous tissue beneath it. (x 6)

The sacro-coccygeal sinus and complications have been described on many occasions and require no special statement here. Although well-known previously, it attracted attention in World War II, being designated "jeep disease". Lumbar sinuses have been described by Hueston (1953) and Aird (1957). The writer has observed sinuses in the crease above the buttock in an obese patient and in the sulcus below the buttock.

An anterior perineal sinus was described by Smith (1948) and peri-anal sinuses have been recorded by Edwards and Reimann (1950). A sinus of the mons veneris immediately above the symphysis pubis, a sinus containing hairs in the clitoris and another at the anterior extremity of the pudendal cleft have been described by Macleod (1953), Palmer (1957) and Thwaite (1957). Palmer (1957) refers to cases which do not contain hair and are probably of a different kind. Hair-containing sinuses of the umbilicus were discussed by Jackson (1854), Aird (1952), Patey and Williams (1956), and Sadeghi-Nejad and Rains (1958).

Sinuses of the hair-bearing area of the face and neck have been observed (Aird, 1957; King, 1947). A sinus between folds of skin of a mid-thigh amputation stump was recorded by Shoesmith (1953). The condition in the sole of the foot was referred to by Hodges (1880) and penetration of the skin of the foot by hairs has been described by Schulze (1950) and Morrell (1957). The interdigital sinus has attracted attention since its description by Patey and Scarff (1946); a review of cases is given by Currie, Gibson and Goodall (1953), Downing (1952) and Hueston (1953).

FIG. II. Photomicrograph of part of the sinus; its lining is stratified squamous epithelium throughout (a break in the deeper part is artefact) and a small amount of debris is present in it. (x 30)

An example of a pilonidal sinus of the axilla was described by Aird in 1952. An associated infection spread through the tissues over a considerable area so that the case presented a serious therapeutic problem. The example to be described here was of minor surgical import; its nature was thus more easily demonstrable.

Pathological features of a sinus

The orifice of the sinus is usually in the depths of a crease or fold in the skin. Although commonly in the deepest part this is not necessarily so and, for example, in the

internatal cleft, the openings may be found occasionally on one side of the midline; this refers to the main orifice and not to secondary openings resulting from infection and bursting of small abscesses which are often lateral.

The size of the sinuses varies greatly. Sometimes small, being only a few millimetres in depth, at other times they extend some distance and are sufficiently commodious to contain much material, usually matted hair. They vary in number; commonly there is one but occasionally, and particularly in the sacrococcygeal region, there may be two or more. This is one of the features which attracted attention to the possibly acquired nature of the condition and also it has a bearing on development of "recurrences" after removal of a sinus.

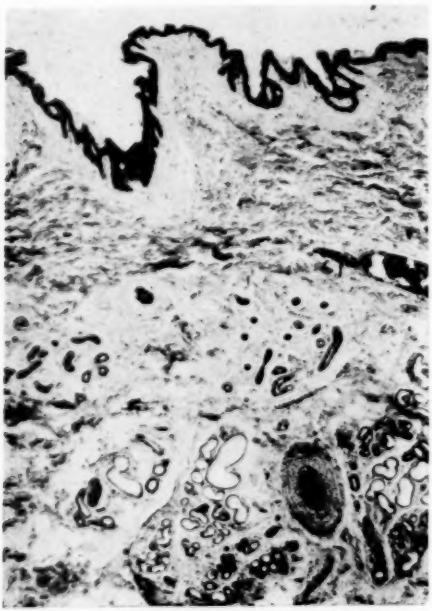


FIG. III. Photomicrograph of the skin adjacent to the sinus showing numerous sudoriferous and apocrine glands and hair follicles. (x 30)

Infection of the sinus is common. It usually causes subacute inflammation of the wall particularly where this is not covered by epithelium; acute exacerbations frequently take place. Infections spread for considerable distances and the sinuses thus become enlarged and often branching in form. Ultimately, from secondary openings in the skin, they become fistulae.

The lining of the sinuses varies. Epithelium from the surface grows into them but often a large part of the wall is lined by granulation tissue in which hair or other material is incorporated. The relative proportion of granulation tissue and epithelium differs and sometimes epithelium may cover practically the whole of the wall.

FIG. IV. Higher power view of portion of the deep aspect of the sinus (from a section serial with that shown in Fig. II). The sinus is lined throughout by squamous epithelium; hair follicles are not present but a hair shaft is visible. (x 60)

Contents of sinuses

The most obvious content is the hair; this attracted attention first and for a long time it was thought to grow in the sinus, but it is now established that it comes from the neighbourhood. Various hypotheses have been developed, in some detail, to account for this entry of hair into the sinus.

The hair is of the same type, colour and texture as that in the neighbourhood. Much

has been said about the orientation of the hairs and it has been noted that frequently the roots (bulbs) are deeply situated, thus appearing at first sight to support the suggestion that they grew in the sinus; but as pointed out by Patey and Scarff this would be expected even if the hairs came from the exterior owing to the orientation of the scales on them. However, this is not invariable; as pointed out by Warren (1854) sometimes they are "inverted" and it should be noted that this was recorded long before controversy as to the mode of development of sinuses arose. Histological examination may demonstrate this inverted arrangement.

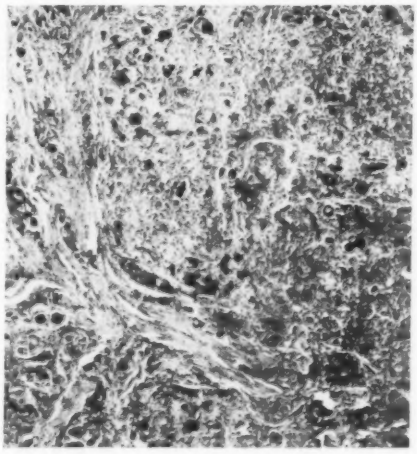


FIG. V. Low power photomicrograph of the granuloma in which numerous foreign body giant cells are present. (x 80)

It is important that apart from debris accompanying hair, the origin of which may be uncertain, other extraneous materials have been observed. Sheep's wool (shown by the histological characters of the fibre surface) has been found in interdigital sinuses of shearers; a case was described by Matheson (1951) and several cases have been observed by the writer. Cattle hairs have been recorded by Becker (1930), dog's hairs by Morrell (1957) and, in a short note in humorous vein, the possibility of vegetable material was referred to by Page (1955).

CASE HISTORY

E.B., a female, married, aged 56, remarked, during a routine follow-up examination for an abdominal operation, that she had had a small painful area in the left axilla over the previous six to eight weeks. It had been red and hard but had improved gradually without special attention.

On examination, a small indurated area in a crease just behind the anterior axillary fold and measuring about 2.5 cm. in diameter was observed. A few hairs were noticed protruding from a small sinus in the middle of the area. The patient's personal hygiene was good and no other lesion of this or other kind was found on the chest or abdominal wall. A talc powder had been applied at intervals to the axilla. The patient thought that the condition was improving but agreed to its removal.

FIG. VI. Photomicrograph, with polarized light, showing spicules of anisotropic material. The prisms were only partially crossed so that the structure of the tissue is demonstrated. The spicules, in general, are related to giant cells. The appearances are characteristic of talc granuloma. (x 180)

Macroscopic appearances

The specimen consisted of an elliptical piece of skin 2 cm. long with underlying fat tissue. There was a small depression in the middle of the skin and from this some hairs protruded. There was a firm thickening in the deeper tissues immediately beneath the skin.

On section through the middle of the specimen, a sinus 6 mm. in length containing a few loose hairs was found. At its fundus there was a fibrous thickened area 5 mm. in diameter fairly well demarcated from the surrounding fat (Fig. I.).

Microscopic appearances

Histologically the skin was normal showing hair follicles and numerous sweat glands (Fig. II.). There were some depressions in the skin and a well-defined sinus which was lined by typical stratified epithelium (Fig. III.). This sinus appeared to be lined continuously throughout by squamous epithelium. There was some debris in the sinus and shafts of hairs were shown in longitudinal section. In the neighbourhood

a crypt, presumably an extension of the main sinus, was present; this contained a hair in section and debris (Fig. IV).

Surrounding this sinus there were collections of small round cells. Beyond the fundus there was a considerable increase in cellularity due to increase in number of spindle cells and accumulation of small round cells; there were also numerous foreign body giant cells (Fig. V). Some material which appeared to be of crystalline nature was observed in the ordinary sections with haematoxylin and eosin staining. Tissues were examined under polarized light and numerous small spiculated areas of anisotropic material were observed (Figs. VI and VII). Some of this was lying free in the tissue but in most cases it was surrounded by multinucleated protoplasmic material constituting the giant cells.

FIG. VII. Photomicrograph with polarized light (partially crossed Nichol prisms) showing the features of the granuloma. (x 180)

DISCUSSION

The site of the sinus in this case highlights the distribution of pilonidal sinuses at positions other than the sacro-coccygeal region; more important, however, is its significance in the mode of development.

There is still difference of opinion, despite the large amount of evidence that has been collected, regarding the general process of formation of the sinuses as is shown by statements in papers that have appeared in the last few years and also in correspondence in current journals (Page, 1955). However, the arguments in favour of an acquired lesion have been put forward clearly recently by such writers as Patey and Scarff (1948), Hueston (1953), and Brearley (1955). Although there are some differences in minor points in the explanations given (and, indeed, there may be differences in the precise mode of formation in different cases), the proposition that there are changes in pressures in the depths of a sulcus or crease during movements of the adjacent tissues and that this may cause a suction action, by which material is drawn into the depths and into any *cul-de-sac* which may be present, appears irrefutable.

In this case, the site of the sinus in a sulcus just beneath the anterior axillary fold supports the general suction hypothesis. A hair or sharp body could penetrate the normal skin, particularly when this became softened (as it may well do in the axillary region) or, on the other hand, a hair follicle or sweat gland may be the point at which some material may enter from without, especially when one considers the ease with which hairs enter the small orifices of an electric razor. Once the opening is formed (or a natural space entered) the foreign body or bodies will facilitate infection and enlargement of the opening.

There has been considerable discussion about the orientation of the hairs in the sinus. However, it is not necessary to depend on this feature to demonstrate that material is actually sucked into the sinus. Debris of various kinds may be found as well as hairs and sheep's wool and cattle and dog hairs clearly indicate their extraneous origin.

In the present case the talc granuloma at the fundus of the sinus is further indication of the mode of development of, and external origin of material in, the sinus. Talc powder had been used and the distribution of the material and cellular reaction indicate that considerable material had entered the area. There is no history to suggest any direct injury such as an incision of the skin. Whether the sinus was at one period deeper and, prior to the time of examination, talc material entered into the depths with subsequent partial healing is uncertain; whether it passed into small crypts (such as were shown histologically to be present in the deeper parts) and then sharp crystals were mechanically propelled through the epithelium (or even into the lumens of sudoriferous glands) or through granulation tissue that was not epithelialized, cannot be determined.

The clinical history as well as the histological appearances suggest that the lesion is not an ancient one, so that here again, especially in view of the age of the patient, there is the indication that the condition has an acquired origin. The well-epithelialized lining of the sinuses might cause momentary doubt as to the mode of origin until it is remembered how easily and rapidly sinuses in various parts of the body, lined by granulation tissue, become lined by well-differentiated epithelium.

The general question of whether conditions are due to preformation or epigenesis, that is to say, whether they are genetic or environmental in origin, is an important one which has been answered in recent years in the direction of recognition of the importance of acquired factors in many fields. An important practical point is that if environmental factors are so important the way is made clear for their control. It is therefore astonishing that the rigid viewpoint of the "congenital" origin of many conditions should have held sway for so long.

SUMMARY

A typical pilonidal sinus occurring in the axilla is described. It contained hair and there was, at its apex, a characteristic talc granuloma.

Not only did the position of this sinus support the general view of the acquired nature of these sinuses but the granuloma indicated that the contained material did in fact enter the region (and the sinus) from the exterior.

ACKNOWLEDGEMENT

I am indebted to Mr. Paul Jones for the specimen and clinical notes of this case.

REFERENCES

AIRD, I. (1952), *Brit. med. J.*, vol. I, page 902.

—— (1957), "A Companion in Surgical Studies." Edinburgh and London, E. and S. Livingstone Ltd.

BECKER, E. (1930), *Chirurg*, vol. 2, page 708.

BREARLEY, R. (1955), *Brit. J. Surg.*, vol. 43, page 62.

CURRIE, A. R., GIBSON, T., and GOODALL, A. L. (1953), *Brit. J. Surg.*, vol. 41, page 278.

DOWNING, J. G. (1952), *J. Amer. med. Ass.*, vol. 148, page 1501.

EDWARDS, M., and REIMANN, D. L. (1950), *Amer. J. Surg.*, vol. 80, page 929.

HODGES, R. M. (1880), *Boston Med. Surg. J.*, vol. 103, page 485.

HUESTON, J. T. (1953), *Brit. J. Surg.*, vol. 41, page 307.

JACKSON, quoted by WARREN, J. M., *loc. cit.*

KING, E. S. J. (1947), *Aust. N.Z. J. Surg.*, vol. 16, page 182.

MACLEOD, R. G. (1953), *Brit. med. J.*, vol. I, page 710.

MATHESON, A. D. (1951), *Aust. N.Z. J. Surg.*, vol. 21, page 77.

MORRELL, J. F. (1957), *Arch. Derm.*, vol. 75, page 269.

PAGE, B. H. (1955), *Lancet*, vol. I, page 873.

PALMER, E. (1957), *Amer. J. Surg.*, vol. 93, page 133.

PATEY, D. H., and SCARFF, R. W. (1946), *Lancet*, vol. 2, page 484.

——, —— (1948), *Lancet*, vol. 2, page 13.

—— and WILLIAMS, E. S. (1956), *Lancet*, vol. 2, page 281.

SADEGHI-NEJAD, H., and RAINS, A. J. H. (1958), *Lancet*, vol. I, page 567.

SCHULZE, H. A. (1950), *Arch. Derm.*, vol. 61, page 618.

SHOESMITH, J. H. (1953), *Lancet*, vol. 2, page 378.

SMITH, T. E. (1948), *J. Amer. med. Ass.*, vol. 136, page 973.

THWAITE, T. J. (1957), *Aust. N.Z. J. Surg.*, vol. 27, page 67.

WARREN, J. M. (1854), *Amer. J. Med. Sc.*, vol. 28, page 113.

FATAL COMPLICATIONS FOLLOWING COLECTOMY*

By E. S. R. Hughes

Royal Melbourne Hospital, Melbourne

A SMOOTH convalescence is the rule after partial or complete colectomy, and this despite inclusion of patients who would have been rejected as unfit a decade ago. However, it is not always the "poor risk" patient who develops fatal complications, a point to be emphasized because it is unwise to assume that the mortality associated with this surgery cannot be reduced.

In this investigation the cause of death in a personal series of cases subjected to colectomy has been analysed. All cases treated by the writer to April 1958 have been included.

Present Series

A total of 602 patients have been subjected to partial or complete colectomy for various reasons (Table 1). Of these, 36 (6.0 per cent.) died as a result of the operation (Table 2). One succumbed on the thirty-first day and another on the fiftieth day after operation, but the remaining patients died in the first four weeks after operation.

1. Carcinoma of the Rectum (336 cases)

Tumours of the anus and anal canal have been included, but not those of the recto-sigmoid segment (15 to 18 cm. from the anus). A synchronous combined excision of the rectum was performed in 249 instances, abdomino-perineal excision in 38, anterior resection and anastomosis in 37, and abdomino-anal "pull-through" anastomosis in 12. In the same period 27 patients were rejected as unsuitable for excision (approximately 92 per cent. resectability rate).

There were 17 deaths; 12 followed synchronous combined excision (4.8 per cent.), one followed abdomino-perineal excision (2.6 per cent.), two followed anterior resection and end-to-end anastomosis (5.4 per cent) and two followed abdomino-anal anastomosis (16.7 per cent.).

2. Carcinoma of the Colon (148 cases)

There were 148 resections for carcinoma of the colon and recto-sigmoid colon (15 to 18 cm. from the anus). In the same period 15 other cases were found irremovable, to give a resectability rate of just over 90 per cent. There were seven deaths (4.7 per cent.).

Table 1

PERSONAL SERIES OF COLECTOMY

Lesion	*No.*
Carcinoma of rectum	336
Carcinoma of colon	148
Diverticulitis of colon	24
Ulcerative colitis	60
Miscellaneous	
Segmental colitis	9
Benign tumours	8
Familial polyposis	6
Volvulus of sigmoid	5
Carcinoid tumour	2
Endometriosis colon	2
Injury	1
Constipation	1
TOTAL	602

3. Diverticulitis of the Sigmoid Colon (24 cases)

In 24 instances the sigmoid and recto-sigmoid colon were removed for diverticulitis. There were five deaths (20.8 per cent.). In 20, a one-stage resection and anastomosis was performed with two deaths; in four, resection followed a previous transverse colostomy and three died (75 per cent.).

4. Ulcerative Colitis (60 cases)

Partial or complete colectomy for ulcerative colitis was carried out in 60 patients with six deaths (10 per cent). In 57 an ileostomy

* Delivered at the Annual Meeting of the Royal Australasian College of Surgeons at Perth, August, 1958.

was constructed and the colon removed (one or more stages) and five patients died. In four, colectomy and ileo-rectal anastomosis was performed and one patient died.

5. Miscellaneous Conditions (34 cases)

Colectomy was performed in nine patients with segmental colitis, in eight with benign tumours, in six with familial polyposis, in five with volvulus of the colon, in two with carcinoid tumour, in two with endometriosis of the large bowel, in one with injury, and in one with constipation. There was one death amongst these 34 cases (a patient with volvulus of the sigmoid colon died on the seventh post-operative day from pulmonary embolism).

CAUSE OF DEATH IN THE PRESENT SERIES (Table 3)

1. Pulmonary embolism (9 deaths)

Pulmonary embolism accounted for nine deaths (1.5 per cent.). Fatal embolism followed excision of the rectum on four occasions, right hemicolectomy for carcinoma on three, procto-colectomy for ulcerative colitis on one, and excision of the sigmoid colon for volvulus on one (Table 4).

Eight of the nine patients were males. The ages of the patients were 67, 72, 71, 71, 44, 65, 72, 65 and 75 years, respectively. The patient who was aged 44 years died after ileostomy and procto-colectomy for ulcerative colitis.

TABLE 2

MORTALITY RATE FOLLOWING COLECTOMY FOR VARIOUS CONDITIONS

Procedure	*No. Cases*	*No. Deaths*	*Percentage Mortality*
Carcinoma rectum: synchronous combined excision	249	12	4.8
Carcinoma rectum: abdomino-perineal excision	38	1	2.6
Carcinoma rectum: anterior resection and anastomosis	37	2	5.4
Carcinoma rectum: abdomino-anal anastomosis	12	2	16.7
Carcinoma recto-sigmoid: resection and anastomosis	16	1	6.3
Carcinoma sigmoid: resection and anastomosis	55	1	1.8
Carcinoma descending colon: resection and anastomosis	13	0	0.0
Carcinoma splenic flexure: resection and anastomosis	13	0	0.0
Carcinoma transverse colon: resection and anastomosis	9	2	22.2
Carcinoma hepatic flexure: resection and anastomosis	8	0	0.0
Carcinoma ascending colon: resection and anastomosis	18	1	5.6
Carcinoma caecum: resection and anastomosis	16	2	12.5
Diverticulitis sigmoid: one-stage resection and anastomosis	20	2	10.0
Diverticulitis sigmoid: resection after preliminary colostomy	4	3	75.0
Ulcerative colitis: ileostomy and procto-colectomy	37	4	10.8
Ulcerative colitis: staged removal colon	20	2	10.0
Ulcerative colitis: other procedures	3	0	0.0
Miscellaneous colectomy	34	1	2.9
TOTAL	602	36	6.0

Five of the patients were postured on the Lloyd-Davies stirrups at the time of the operation. The operation in each case was uneventful, and was carried out in reasonable time and without shock. Early post-operative movements were encouraged. Except for one patient who had a residual abscess and a partial small bowel obstruction, death was unexpected. Leg pain did not occur and none complained of pleuritic pain, suggestive of small infarction, in the days preceding the massive embolism. The average time between operation and fatal embolic episode was ten days.

TABLE 3

CAUSE OF DEATH FOLLOWING COLECTOMY

Cause of Death	*No. of Cases*
Pulmonary embolism	9
Peritonitis	7
Small bowel obstruction	6
Pneumonia	5
Other causes	9
TOTAL	36

2. Peritonitis (7 deaths)

Peritonitis was responsible for the loss of seven patients (Table 5). It occurred only in those patients in whom there was an intra-abdominal anastomosis, and in each case the peritonitis appeared directly related to that anastomosis.

Fatal peritonitis occurred in three of 49 restorative resections performed for carcinoma of the rectum (tumours lying within 15 cm. of the anal margin). In two of these the peritonitis was the sequel of an abdomino-anal (pull-through) anastomosis for low-lying tumours, and in one (not confirmed by autopsy) it complicated anterior resection and anastomosis in an obese individual.

Peritonitis appeared responsible for the loss of two of the five patients dying after resection for diverticulitis. Both patients had had a colostomy established some time prior to the resection.

Peritonitis caused the loss of one patient after colectomy and ileo-rectal anastomosis for ulcerative colitis. A temporary ileostomy had been established three months before.

Only one patient died from peritonitis in 148 resections and intraperitoneal anastomoses for carcinoma of the colon and recto-sigmoid segment. This patient had had a transverse colostomy performed for an obstructing tumour of the splenic flexure. At the second operation two weeks later the tumour and the colostomy were resected together and the remaining transverse colon anastomosed to the descending colon. Complete separation of the suture line occurred.

3. Small bowel obstruction (6 deaths)

Small bowel obstruction was responsible for the loss of six patients and in five of these the initial operation was an abdomino-perineal excision of the rectum (Table 6).

In three of the patients the small bowel had herniated through the pelvic peritoneal suture line. In a fourth, the small bowel was adherent to the region of the inferior mesenteric vascular ligature and it was thought that herniation through the upper end of the pelvic peritoneal suture line had occurred. In a fifth patient fibrinous adhesions were responsible for the obstruction. In the sixth patient the small bowel had become adherent to the peritoneal suture line which resulted from closure of the lateral space following ileostomy and procto-colectomy. In three of the patients a laparotomy designed to relieve the obstruction was performed a few days before the patient died.

4. Pneumonia (5 deaths)

Pneumonia was responsible for the loss of five patients. In one of these a lung abscess complicated a thoracic aneurysm.

Mr. N.R. (R.M.H. 147,694), aged 63 years, was admitted to hospital with a large bowel obstruction caused by a carcinoma of the rectum. He had been gassed in the first world war and had an aortic aneurysm of specific aetiology. On 22 July, 1953, a caecostomy was performed and on 14 August, 1953, a synchronous combined excision of the rectum. His condition was satisfactory throughout the operation, although the anaesthetist had difficulty in keeping the patient a good colour. One litre of blood was transfused during the operation. During the evening of the day of operation there was a sharp blood loss from the perineal wound,

causing a fall in blood pressure. The following day the skin around the colostomy became inflamed and areas necrotic; on the second post-operative day portion of the colostomy sloughed and on the third day a bed-sore appeared over the sacrum and urine commenced to drain through the perineal wound. Moist sounds appeared in the chest and he deteriorated slowly to die on 20 August 1953. Autopsy revealed a lung abscess which had ruptured into the pleural cavity to form an empyema. A large thoracic aortic aneurysm was present. The abdominal cavity was clear.

no organic obstruction was found. After this second operation his condition fluctuated, but on the whole he progressed favourably. By 28 April, he seemed satisfactory, although his blood pressure (120/70) was considerably lower than the pre-operative level. The chest was clear and the urinary output normal. That night he died suddenly.

Autopsy revealed basal bronchopneumonic consolidation in both lungs and a small infarct in the upper lobe of the right lung. The remainder of the autopsy examination was normal, including examination of the gastro-intestinal tract.

TABLE 4

FATAL PULMONARY EMBOLISM FOLLOWING COLECTOMY

No. Case	*Pat.*	*Sex*	*Age*	*Condition*	*Operation*	*Date Op.*	*Date Death*	*No. Days Post-op.*	*Comment*
1	E	M	67	Ca. rectum Second liver	Abdo.-perin. exc.	25.3.51	6.4.51	12	Sudden, in bathroom on day of discharge from hospital
2	M	M	72	Ca. rectum	S.C.E.	29.3.53	6.4.53	8	Sudden, in bed, after uneventful convalescence
3	M.S.	M	71	Volvulus sigmoid	P.M. resection	7.8.53	15.8.53	8	Sudden, after uneventful convalescence
4	L.M.	M	71	Ca. rectum	S.C.E.	17.8.54	29.8.54	12	Sudden, early hours morning
5	L.D.	M	44	Ulcerative colitis	Ileostomy; proctocolectomy	23.12.54	4.1.55	12	Sudden, in bath
6	B	F	65	Ca. rectum	S.C.E.	9.4.55	27.4.55	18	Sudden, whilst having lunch at home
7	N	M	72	Ca. caecum	Right hemicolectomy	27.7.55	3.8.55	7	Sudden, walking back to bedroom after bath
8	B	M	65	Transverse colon	R. hemicolectomy	21.3.57	30.3.57	9	Had been sick from residual abscess and partial ileus
9	S	M	75	Ca. caecum	R. hemicolectomy	26.8.57	31.8.57	5	Sudden, sitting in chair talking to nurse

Mr. N.B. (R.M.H. 167,779), aged 74 years, was admitted to hospital on 10 April 1956. For two or three years he had been passing blood from the rectum. He was vague and it was difficult to obtain a detailed account of his illness. Examination revealed hypertension (210/110) and emphysematous lungs. There was a protuberant tumour 15 cm. from the anus.

On 17 April 1956, under thiopentone, tubarine and nitrous oxide anaesthesia, he was submitted to anterior resection and anastomosis. The tumour appeared to be a low grade carcinoma, confined to the bowel. The pulse and blood pressure showed no significant variation during the operation.

For the first two days his condition was good. On 20 April 1956, he fell out of bed reaching for a book. The same evening he complained of colicky lower abdominal pain. His pulse rate rose to 120 beats per minute and he developed shortness of breath. The chest appeared normal clinically. The abdomen became tender and a little distended. He improved, but had a further episode of colicky abdominal pain on the following day. On 22 April, large quantities of bile-stained fluid were aspirated from his stomach and laparotomy was done the same evening. The small bowel was distended, but

Mrs. C.R. (Private patient referred by Dr. Green) was admitted to the Intermediate section of the Royal Melbourne Hospital for investigation of rectal bleeding. Blood loss continued after admission to hospital and several transfusions were given before a decision was made in favour of laparotomy. On 19 April 1957, under thiopentone, tubarine and nitrous oxide, laparotomy was performed and it disclosed an area of diverticulitis involving the sigmoid colon. There was no other lesion. The affected portion of the colon was removed and an end-to-end anastomosis constructed. The operation proceeded without complication.

In the post-operative period the patient was weak, but otherwise appeared satisfactory. Her abdomen was soft, without distension. She failed to regain strength and died of bronchopneumonia on the eleventh post-operative day. No autopsy was performed.

Mr. J.C. (R.M.H. (176,547), aged 68 years, was admitted to the Royal Melbourne Hospital on 2 July 1957, for investigation of a colicky lower abdominal pain and increasing constipation of twelve months' duration. His symptoms had become worse and for a few days before his admission he was greatly distressed.

His physique was fairly satisfactory and the cardiovascular system within normal limits for a man of his age. The liver was enlarged and a large hard irregular mass palpable above and to the left of the pubis was thought to be malignant. The presence of blood-stained mucus in the lumen of the rectum supported such a diagnosis.

was tender and perhaps a little distended. However, by 8 October, his condition was satisfactory; his mental condition had returned to normal, the urinary output had recovered, and the chest was clear of physical signs. The blood urea was 65 milligrams per cent. and the haemoglobin level 95 per cent. Two days later he became mentally confused once

TABLE 5

FATAL PERITONITIS FOLLOWING COLECTOMY

No.	*Case*	*Sex*	*Age*	*Condition*	*Operation*	*Date*	*Cause of Complication*	*Death*	*Days Post-Op.*
1	B	M	71	Diverticulitis with abscess. Transverse colostomy 18/12 before.	Resection sigmoid and anastomosis	24.11.52	? separation suture line	6.12.52	12
2	L	F	86	Carcinoma rectum.	Abdominal resection. Trans-anal anastomosis	15.7.53	? separation suture line	22.7.53	7
3	M.W.	F	27	Ulcerative colitis, Ileostomy 6/52 before, on 22.12.53	Colectomy and ileo-rectal anastomosis	2.2.54	Separation suture line	24.3.54	50
4	H	F	64	Carcinoma splenic flexure. Had transverse colostomy for acute obstruction (16.2.54)	Resection tumour and colostomy, and anastomosis	1.3.54	Separation suture line	15.3.54	14
5	L	M	65	Diverticulitis. Transverse colostomy 30/12 before	Resection sigmoid colon and anastomosis	14.11.56	? separation suture line	21.11.56	7
6	C	M	76	Carcinoma rectum	Abdominal resection. Trans-anal anastomosis. Trans. colostomy	24.1.57	Separation suture line	9.2.57	16
7	R	M	63	Carcinoma rectum	Abdominal resection and anastomosis	2.8.57	? peritonitis	9.8.57	7

On 11 July, under pentothal, tubarine, and nitrous oxide, a laparotomy was performed. The mass in the pelvis appeared to be a carcinoma originating in the sigmoid colon. The affected portion of the bowel was removed and an end-to-end anastomosis constructed deep in the pelvis. The operation was uneventful and for the first two days after operation his condition was good. On the third post-operative day his temperature rose, he became dyspnoeic and he started to cough up large quantities of whitish sputum. An X-ray of his chest was normal. His condition deteriorated and within a few hours he became disorientated and finally unconscious. He died on 16 July 1957, five days after operation. Autopsy showed that the lower lobes of both lungs were grossly congested with areas of consolidation. There was no evidence of pulmonary embolism or infarction. The heart was within normal limits. The peritoneal cavity was clear, the suture line was intact, and there was no evidence of peritonitis. Asian influenza virus (epidemic at the time of the operation) was isolated from the bronchial washing, and numerous staphylococci were present.

Mr. C.S. (R.M.H. 178,178), aged 81 years, presented with a carcinoma of the rectum, 10 cm. from the anus. On 1 October 1957, an anterior resection and end-to-end anastomosis was performed under thiopentone, tubarine and nitrous oxide anaesthesia administered through a cuffed orotracheal tube. The operation was completed without incident. The following day he was mentally confused with basal crepitations at both lung bases. His urinary output for the first two or three days was lower than was to be expected and his abdomen again; basal crepitations reappeared and he developed diarrhoea. He did not respond to treatment and died on 16 October. Autopsy revealed bronchopneumonia involving the lower lobes of both lungs, especially the left side. There was no evidence of pulmonary infarction. Some gastric contents were present in both bronchi, but this was thought to be a terminal aspiration. The intestinal tract was normal.

5. Other causes of death (9 cases)

Enterocolitis (1 case)

Mr. C., aged 62 years (private case referred by Dr. B. Botterill) was admitted to hospital for elective surgery for carcinoma of the descending colon. He was short and very obese. On 18 June 1954, a left hemicolectomy was performed and the transverse colon anastomosed to the recto-sigmoid segment. Operation was uneventful and for the first two days his condition was good. On the third day his pulse rate rose, the abdomen became distended, and profuse vomiting and diarrhoea commenced. Continuous gastric suction produced large volumes of greenish brown fluid and a similar fluid poured at frequent intervals from the rectum. Staphylococcus aureus was identified in this rectal discharge. His condition showed a steady decline and he died on 26 June, eight days after operation. He was given phthalylsulphathiazole before operation, and penicillin and streptomycin afterwards. A final diagnosis of staphylococcal enterocolitis was made, but no autopsy examination was made.

Bacteriaemia (1 case)

Mrs. R. (R.M.H. 161,699), aged 40 years, was admitted to the Royal Melbourne Hospital with ulcerative colitis. The condition had been present intermittently for eleven years; the last exacerbation had commenced two months before her admission. She failed to respond to medical treatment and accordingly on 8 June 1955, ileostomy with subtotal colectomy was performed.

Her condition appeared satisfactory immediately after this procedure and at the end of the first week she was taking a light diet and felt fairly comfortable. However, transfusion wounds on the forearm became infected, a persistent irregular pyrexia developed and an ulcerative stomatitis appeared.

Staphylococcus aureus (coagulase positive) was cultured from the blood, from the cerebro-spinal fluid, from the urine and from the rectal stump. Her condition deteriorated, she became confused and later comatose, to die on 30 June.

Autopsy revealed tiny metastatic abscesses in all parts of the body, including the brain.

Pericarditis (1 case)

Mr. S.B., aged 70 years, was admitted for surgical treatment of a carcinoma of the rectum. The day before operation he developed influenza (epidemic at the time). Operation was cancelled and for a few days he was very ill. His temperature was elevated and he became very weak. He was discharged from hospital and two weeks later re-admitted.

After preparation for five days a synchronous combined excision of the rectum was performed. He collapsed in an early stage of the operation. Thick mucopus was aspirated from the right bronchus. His condition was poor on the night of the operation and he deteriorated further on the following day. His pulse became rapid and irregular and he died on the second post-operative day, a few hours after a temperature of 105 degrees Fahrenheit was recorded.

Autopsy revealed acute pericarditis. There was bilateral pulmonary congestion.

Uraemia (1 case)

Mrs. A., aged 65 years (referred by Dr. Roman Zeeher) had had a transverse colostomy for diverticulitis of the sigmoid colon performed eight years previously. She had had attacks of cystitis over the past twelve months. She was very short, very obese and her urine was heavily loaded with albumin. Renal function tests confirmed damage to the kidney.

On 13 February 1957, the sigmoid colon was excised. Portion of the bladder was removed because the colon was adherent to it, and subsequent examination showed the presence of a vesico-colic fistulous communication.

She was well for a few days after which her urinary output gradually decreased until in the second week she was passing only 50 to 60 cc. of urine per day. This continued for a further ten days before she finally succumbed three weeks after operation.

Cerebro-vascular accident (1 case)

Mr. B., aged 42 years (referred by Dr. J. Champion de Crespigny) was first seen in 1953 with large third degree haemorrhoids which were removed. He remained well until 1955 when he reported with a recurrence of bleeding. Examination showed proctitis to 10 cm.; above this the bowel was normal. Over the next two years the inflammation extended up the large bowel. An acute exacerbation was responsible for an emergency admission to hospital in March, 1958, and on 1 April 1958, an ileostomy and procto-colectomy was performed. The procedure was accomplished without untoward incident and there was a substantial improvement in his general condition on the following day. On the morning of 3 April, he could not be aroused completely and he was found to have a left sided hemiplegia. During the next day his mental condition fluctuated between one of confusion and complete coma. He appeared to improve on 6 April, but relapsed into a deep coma from which he could not be roused and he died on

TABLE 6

FATAL SMALL BOWEL OBSTRUCTION FOLLOWING COLECTOMY

No.	*Case*	*Sex*	*Age*	*Condition*	*Operation*	*Date*	*Cause of Obstruction*	*Treatment*	*Date Death*	*Days Post Op.*
1	J.P.	M	70	Carcinoma rectum	S.C.E.	24.6.49	Adherence to site ligature of inferior mesenteric vessels	Expectant	4.7.49	10
2	T.Y.	M	82	Epithelioma anus	S.C.E.	19.11.53	Herniation through pelvic peritoneal suture	Expectant	30.11.53	11
3	F	F	26	Carcinoma rectum	S.C.E.	8.12.53	Herniation through pelvic peritoneal suture	Laparotomy 15.12.53	18.12.53	10
4	L.W.	F	62	Carcinoma rectum	S.C.E.	19.1.54	Fibrinous adhesions	Laparotomy 25.1.54	27.1.54	8
5	W.K.	M	61	Carcinoma rectum	S.C.E.	15.10.54	Herniation through pelvic peritoneal suture	Expectant	25.10.54	10
6	K	M	26	Ulcerative colitis	Ileostomy procto-colectomy	28.2.56	Herniation through lateral space suture	Laparotomy	1.4.56	31

8 April. His abdomen remained satisfactory during this week and although no autopsy was obtained death seemed to be due to cerebral thrombosis.

Adrenal insufficiency (1 case)

Mrs. E.L. (R.M.H. 161,746), aged 62 years, developed diarrhoea quite suddenly two months before her admission to hospital. The diarrhoea was associated with the passage of blood and had been persistent. Sigmoidoscopy showed severe ulcerative colitis. She deteriorated after admission to hospital. On 10 June 1955, 100 milligrams of cortisone was given and over the next few days this dose was reduced to 25 milligrams twelve-hourly. Her condition showed no improvement and, accordingly, on 23 June, ileostomy and procto-colectomy was performed. She tolerated operation well and on the following day appeared to be much improved. However, twenty-seven hours after operation she collapsed and died. Autopsy showed oedema of the suprarenal gland and in the cortex many degenerative and atrophic cells. As no cortisone was given during or after operation it was believed that death was due to acute adrenal insufficiency (Patricia Wilson, 1956).

TABLE 7

CARCINOMA OF RECTUM

Excision with Colostomy

Series	*No. Cases*	*No. Deaths*	*Percentage Mortality*
1947-1954, Oct.	165	13	8
1954, Oct.-1958, April	122	0	0
TOTAL	287	13	4.5

Uncertain (3 cases)

In two patients subjected to excision of the rectum and in a third who had undergone right hemicolectomy, the cause of death was not established.

Mrs. S., aged 54 years, had a history of ulcerative colitis of ten years' duration and presented with a carcinoma of the rectum of high-grade activity. Her condition was poor and considerable preliminary preparation was necessary before it was possible to carry out an abdomino-perineal excision of the rectum. At operation secondary deposits were felt in the liver and in the omentum. She progressed fairly well until twenty-one days after the operation when she collapsed with severe upper abdominal pain. She lost consciousness within a few minutes and died thirty-six hours later. The cause of death was not established.

Mr. L., aged 35 years, of subnormal intelligence, presented with a carcinoma of the rectum. Synchronous combined excision was performed on 1 June 1953. His operative and immediate post-operative course was satisfactory, but after the third post-operative day he lapsed gradually into confusion, stupor and finally coma and died on 8 June, seven days after operation. The cause was not established.

Mrs. B., aged 77 years, presented with a colicky abdominal pain caused by a carcinoma of the ascending colon. Her general condition was good. On 27 December 1957, a right hemi-colectomy was performed with removal of the glands along the vena cava and aorta. An end-to-end anastomosis was constructed. Her course was satisfactory for four or five days; she then became a little distended, but this appeared to subside and she returned to her home on the tenth post-operative day. Two days later she was readmitted to hospital in a weak condition and with abdominal distension and considerable breathlessness. An X-ray of the abdomen and chest were normal. There was evidence of haemorrhage. Her bowels were active. She deteriorated, to die on 16 January 1958, twenty days after the operation.

TABLE 8

ULCERATIVE COLITIS

Ileostomy and Colectomy with or without Excision of Rectum

Series	*No. Cases*	*No. Deaths*	*Percentage Mortality*
6.10.53-28.2.56	15	4	26.7
19.6.56-1.4.58	34	1	2.9
	49	5	10

DISCUSSION

Improved results are to be expected as surgical experience grows and familiarity with procedure increases. This has proved so with combined excisions of the rectum for carcinoma and also with ileostomy and proctocolectomy for ulcerative colitis.

The last patient lost after a synchronous combined excision of the rectum for carcinoma was on 15 October 1954, and exactly 100 such procedures have been performed since then. In this latter period an additional 22 abdomino-perineal excisions (Miles) have been completed without loss (Table 7). During the whole series a resectability rate of

just over 90 per cent. has been maintained, and in the last 122 cases it has been 94 per cent. In this time nine patients over 80 years (oldest, 89 years) have been treated surgically. This procedure, although of some magnitude, carries a negligible mortality.

In the first ten one-stage ileostomy-proctocolectomy operations for ulcerative colitis there were three deaths, but 27 more were performed in the next two years before the fourth occurred, and the series included desperately ill patients. There has been one death after 12 ileostomy-subtotal colectomies. The last 34 ileostomy-colectomy (with or without excision of the rectum) have been performed with one death (Table 8). The numbers here are small, but the mortality rate with both subtotal colectomy and proctocolectomy excisions has reached a low level.

Although there has been a notable improvement in the results of these operations, this has not been obvious when the colectomy has been associated with an anastomosis. In 1953, 1954 and 1955, a series of 18 restorative excisions of the rectum was performed without loss; in 1957, 19 such operations were followed by three post-operative deaths. In 1956, 31 resections of the colon and recto-sigmoid junction were performed with one death, but in 1957 there were three deaths in 30 such resections (Fig. 1).

There have been five colectomy-ileo-rectal anastomosis procedures for ulcerative colitis (including segmental colitis) and one patient died following partial disruption of the suture line. This loss has prejudiced the writer against this operation, but it is the poor functional result associated with it which has forced him to abandon it except when the rectum is normal.

Results in resection of the sigmoid colon for diverticulitis have been disappointing. In 20, a one-stage resection and anastomosis was performed with two deaths, but in four resection followed a preliminary colostomy and three died. In the same period the writer operated upon 20 patients with diverticulitis complicated by peritonitis, by abscess or by chronic inflammatory "tumour" formation and surgery limited to laparotomy with or without drainage. No colostomy was performed. There were no deaths and there was no further trouble from the diverticulitis. As a result of this experience the writer has learnt to be conservative in his indications for excision in this disease, but when resection has been necessary a one-stage operation is preferable including operations for vesico-colic fistula.

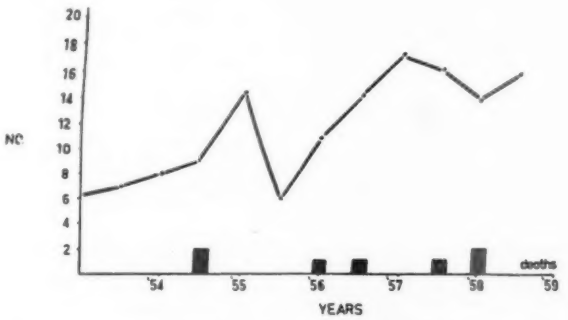


FIG. 1. Mortality associated with colectomy and anastomosis for carcinoma.

Fatal pulmonary embolism

The commonest cause of death in this series was massive pulmonary embolism, occurring on the tenth post-operative day. A study of fatal cases following resection of large bowel tumours at the Lahey Clinic showed that pulmonary embolism and peritonitis were the two conditions most often responsible (Bell, Swinton and Hurxthal, 1957). Buckwalter and his colleagues (1955) stated that eight of 16 deaths following abdomino-perineal excision of the rectum in 176 patients were caused by pulmonary embolism on the ninth day on the average. Goligher (1958) reported that three of 14

deaths following 137 anterior resections for carcinoma were caused by pulmonary embolism. At the Mayo Clinic the operations most often complicated by fatal pulmonary embolism were splenectomies, intestinal resections and hysterectomies (Barker *et alii*, 1940). From 1953 to 1957 inclusive there were 41 cases of autopsy-proven massive pulmonary emboli following operations at the Royal Melbourne Hospital; the most common were large bowel resections, cholecystectomy and prostatectomy (Cuthbertson and Marshall, 1958, in press).

energetically combated, precautions should be taken immediately after operation, even before complete consciousness has been regained. A trained physiotherapist should proceed to massage and perform passive movements of the lower extremity as soon as the patient returns from the theatre, and such attention continued thrice daily until the patient is moving freely.

It is not desirable to give all patients undergoing colectomy post-operative anticoagulant therapy because of the extent of

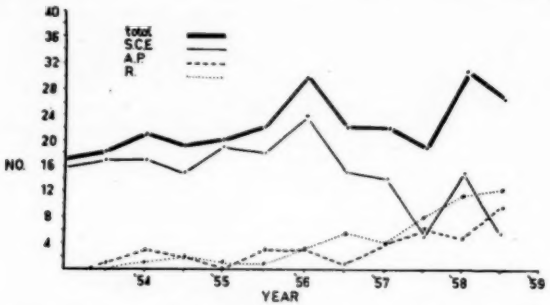


FIG. II. Operations for carcinoma of the rectum. In this graph the change in the author's practice is depicted. (S.C.E., synchronous combined excision; A.P., abdomino-perineal; R., restorative.)

The evidence favours stasis as the important predisposing factor in the cause of thrombosis (Paterson and McLachlin, 1954). Although calf veins have been incriminated as the common origin of the thrombus (Rossle, 1937), it has been demonstrated recently that the upper thigh veins might be responsible more frequently than was believed formerly (Gibbs, 1957). Experimental work (Goble and Hughes, in the press) has shown that insertion of packs and retractors can cause a substantial and sustained rise in the venous pressure of the lower extremity and it is reasonable to postulate that such a rise may be a factor in initiating a thrombosis, either by stasis or by damaging a venule or valve. The incidence of fatal pulmonary embolism might be lowered if packs and retractors are used with care.

It has been the rule in this series to encourage early bed-movements and the patients have been urged to sit out of bed as soon as intravenous therapy has been discontinued. But fatal embolism has still occurred and it seems that if the effects of stasis are to be the raw area after surgery, particularly after abdomino-perineal excision of the rectum. After reviewing the experience in this series, it might be given consideration as an adjunct in the post-operative treatment of males between the ages of 65 and 75 years who require a right hemi-colectomy for carcinoma. Such treatment does not afford complete protection against embolism (De Laughter and Anlyan, 1956). Partial anticoagulant therapy is under trial in some clinics (Allen, 1953; Kistner and Smith, 1954), but the writer has no personal experience as to its efficacy.

Fatal peritonitis

In some published series peritonitis has been a fatal complication after abdomino-perineal excision of the rectum (Postlethwaite *et alii*, 1958), but this has not proved the case in this series where fatal peritonitis has occurred only when there has been separation of the suture line. This happened when the anastomosis proved a difficult technical procedure, because of low situation, because of a contracted bowel surrounded by inflammatory tissue, or because of obesity.

More experience in bowel anastomoses and in pelvic dissections has made it possible to accept increasing numbers of cases for restorative excisions of the rectum, but it is important that judgment be exercised. In many cases it is not possible to decide until operation has progressed for some time as to whether or not restorative procedures or a permanent colostomy will be required (Fig. II). In five of the seven cases of peritonitis in this series a difficult anastomosis was performed deep in the pelvis. Goligher (1958) has had a similar experience; sepsis was the cause of death in five of 14 fatal cases following 137 anterior resections. He found that serious separation of the suture line was almost confined to cases undergoing really low resections.

The broad spectrum antibiotics have not been used in the preparation of the colon in this series. The intestinal sulphonamides have been given in most instances, but these drugs seem of questionable value. It is the writer's practice to carry out an open anastomosis, but precautions are taken to avoid contamination of tissues from the open bowel. Postoperatively penicillin and streptomycin are administered for five days, but a trial without these antibiotics is in progress.

It is interesting to observe the poor results with a preliminary colostomy in this series. Three of four patients with diverticulitis had a preliminary transverse colostomy and two died from what appeared to be peritonitis; the third succumbed from renal failure three weeks after operation. One patient had a carcinoma of the splenic flexure end of the transverse colon causing obstruction. A transverse colostomy was constructed which was later excised with the tumour, but the patient died. This was the only instance of fatal peritonitis in 148 resections and intraperitoneal anastomoses for carcinoma of the colon and recto-sigmoid; excessive traction developed at the suture line, which could have been averted by removal of the whole right half of the colon and anastomosis of the ileum to the sigmoid colon). Another patient had an ileostomy for six weeks before colectomy and ileo-rectal anastomosis was performed, but the operation was followed by partial disruption of the suture line which ultimately proved fatal. In another case a transverse colostomy was done at the time of the abdomino-anal anastomosis for a low-lying carcinoma.

Fatal peritonitis after colectomy appears to be due to faulty technical work which cannot be covered by chemotherapy, antibiotics or proximal colostomy.

Fatal small bowel obstruction

Fatal small bowel obstruction occurred most commonly after abdomino-perineal excision of the rectum. In three of the five fatal cases which followed this operation, the small bowel had herniated through the pelvic peritoneal suture line and in a fourth it was tightly adherent at the site of the ligature of the inferior mesenteric vessels, suggesting a similar mechanism at the upper end of the pelvic peritoneal suture line (Hughes, 1958, in the press).

In each of these cases of Richter's herniae, severe constant abdominal pain was observed from the time of recovery from anaesthesia and it was still present on the second post-operative day. Neither vomiting or distension was an early feature and in fact did not appear for several days. A curious feature which confused the diagnosis was a sharp elevation of the temperature on the second post-operative day.

The complication can be prevented by attention to detail. Before suturing the pelvic peritoneum after abdomino-perineal excision of the rectum, the peritoneum is stripped off the base of the bladder and the side walls of the pelvis, so that the line is free of tension. A continuous interlocking suture, combined with interrupted sutures, prevents the accident. Although some have advocated suturing the peritoneum in such a way as to bring the serous edges into apposition with the free edges downwards, towards the pelvic cavity (Goligher, Lloyd-Davies and Robertson, 1951; Abel, 1957), it is probably more important to suture firmly.

Fibrinous adhesions were responsible for obstruction in a fifth case, but operation was performed too late. In a sixth case a segment of small bowel became adherent to, and possibly herniated through, the suture line resulting from closure of the lateral space after construction of an ileostomy. After this case the writer has made no attempt to close the

space lateral to the ileostomy and there have been no ill effects (41 cases without closure of the lateral space).

These patients with small bowel obstruction were lost because of late surgical intervention. There were several reasons for this. First, most cases of small bowel obstruction occurring in the immediate post-operative period respond to conservative measures and it is difficult to select those patients requiring surgery. Secondly, following large bowel resections, abdominal distension is often regarded as due to obstruction at the anastomosis or at the colostomy; in actual fact, in most such cases the distension is found to be caused by small bowel obstruction. Thirdly, most surgeons are reluctant to re-operate without positive evidence of obstruction.

Fatal pneumonia

Pulmonary infection caused the loss of five patients and in two of these the organism responsible was Staphylococcus aureus. Staphylococcal pneumonia in adults may complicate influenza (Evans and Evans, 1956) or be independent of it. An outstanding feature of staphylococcal pneumonia is the severity of its clinical course and the frequency with which complications occur, such as abscess or empyema (Hausmann and Karlish, 1956). In a series of 14 cases reported by Gresham and Gleeson-White (1957) only four had any kind of acute infection of the lung suspected during life. They urged that the diagnosis be borne in mind whenever there is inexplicable deterioration of the general condition of a debilitated patient. In their cases the organisms concerned were regarded as "hospital" staphylococci and resistant to penicillin, streptomycin and chlortetracycline.

The incidence of fatal bronchopneumonia might be reduced by advising chest physiotherapy for those with diminished lung function. The fluid intake should be restricted in elderly persons to avoid pulmonary oedema. Staphylococcal pneumonia seems more likely to occur in the course of influenzal epidemics, but the diagnosis should be considered in any person who shows a rapid decline with minimal clinical signs to explain the reason. In these patients erythromycin or chloramphenicol should be administered (Gresham and Gleeson-White, 1957).

Other fatal complications

In three cases the cause of death was obscure. In a fourth, acute adrenal insufficiency followed sudden cessation of steroid therapy for ulcerative colitis (described by Patricia Wilson, 1956). A fifth case died of cerebral thrombosis five days after ileostomy and procto-colectomy. In a sixth, uraemia followed resection of the sigmoid colon and portion of the bladder for vesico-colic fistula caused by diverticulitis.

In the remaining three cases staphylococcal infections were present. One died from enterocolitis a week after left hemi-colectomy for carcinoma. A second died of staphylococcal pericarditis on the second day after abdomino-perineal excision of the rectum performed a short while after a preceding influenzal infection. A third died from staphylococcal septicaemia twenty-two days after subtotal colectomy and ileostomy for acute ulcerative colitis. Staphylococcal organisms were identified in the lungs of two patients dying of pneumonia. This means that this organism has been responsible for the loss of probably five patients in this series. These cases have been distributed evenly through the series. They serve to emphasise the gravity of staphylococcal infections.

Although operative procedures on the bowel predispose to ready contamination of the wound, this should not lead to any relaxation of the usual precautions in regard to aseptic surgery. Colonic surgery may be complicated by staphylococcal infections which may prove fatal. Caswell and his colleagues (1958) demonstrated that special attention to aseptic techniques appreciably lower the incidence of wound infection. These authors came to the conclusion that the most important source of contamination was direct transference rather than by nasal carriers or through airborne sources. Strict operating room discipline and careful post-operative dressing techniques should be enforced.

CONCLUSIONS

The cause of fatal complications after colectomy can often be traced to a technical flaw in the course of surgery.

1. It is possible that the incidence of pulmonary embolism can be reduced by gentle and more deliberate insertion of abdominal packs, and by not placing

retractors over the inferior vena cava or over the iliac and femoral veins. Physiotherapy should be instituted as soon as the patient has reached the ward and reliance should not be placed on the nurses' attention or on early ambulation.

2. Fatal (but, of course, not non-fatal) peritonitis is due in almost all cases to partial separation of a suture line. Such a complication is caused by faulty technique, and in most cases is due to difficulty in anastomosing deep in the pelvis or to the performance of an anastomosis without precautions to avoid traction.

3. Fatal small bowel obstruction is caused in most cases by technical and diagnostic error. It is important not to leave a defect through which small bowel can herniate and equally important to intervene promptly if the complication is suspected. Atypical clinical features are the rule.

4. Fatal pneumonia is relatively uncommon. It may occur during influenzal epidemics. It may also be predisposed by excessive intravenous therapy in the elderly. The rapid clinical course in some cases may cause confusion. If a patient shows a sudden decline with minimal clinical signs to explain the reason, the diagnosis should be suspected and a course of erythromycin or chloramphenicol given.

5. Other causes of operative mortality exist, but the most significant are those due to Staphylococcal infections. Even though the operative field is often contaminated from the open large bowel it is important that strict aseptic precautions be adopted throughout the course of surgery.

SUMMARY

1. A personal series of 602 colectomies performed for various reasons has been reviewed to determine the mortality rate, and the causes of death.

2. Combined excision of the rectum showed a mortality of 2.6 per cent. for abdomino-perineal excisions (Miles) and 4.8 per cent. for the synchronous combined excision. In the last 122 combined excisions there have been no deaths. Restorative excisions were followed by a similar mortality except when attempts were made to remove very low lying tumours.

3. Carcinoma of the colon with intraperitoneal anastomosis was associated with an operative mortality of 4.7 per cent.

4. There was a high mortality rate after resection of the sigmoid colon for diverticulitis, especially when a preliminary colostomy had been constructed.

5. Ulcerative colitis was also responsible for a higher mortality rate after excision than was found with carcinoma, but the results of surgery have improved.

6. Increased experience produced a very significant fall in the mortality rate after resection of the rectum and construction of a permanent colostomy; a similar improvement was not found in carcinoma of the colon.

7. The commonest cause of death in this series was pulmonary embolism. Most authorities have continued to stress the importance of stasis as the cause. Experimental work has demonstrated a considerable rise in venous pressures in the lower extremity when packs are inserted and retraction applied.

8. Peritonitis occurred after intraperitoneal anastomosis. It was not responsible for the loss of any patient after construction of a permanent end-colostomy in the course of combined excision of the rectum. Peritonitis became a serious factor when attempts were made to carry out an anastomosis deep in the pelvis and when technical difficulties were considerable. Defective anastomosis rather than an inadequately prepared bowel appeared responsible.

9. Small bowel obstruction was the third common cause of a fatal outcome. It was seen most often after an abdomino-perineal excision of the rectum and in most cases was caused by herniation of the small bowel through an imperfectly sutured pelvic peritoneum. Symptoms appeared immediately after operation and were often accompanied by a confusing rise in temperature. Diagnosis was difficult and this led to late intervention.

10. Pneumonia was the cause of death in five patients, and one of these developed a lung abscess. Pneumonia seems to occur if there have been previous lung disorders, if the patient has had operation during an influenzal epidemic, or if the patient is debilitated. Staphylococcal pneumonia may overwhelm the patient very quickly. The diagnosis should be entertained if there is a sudden and unaccountable deterioration of the patient and erythromycin or chloramphenicol given.
11. Operating room technique must be disciplined in colonic surgery as in any "clean" surgery because fatal staphylococcal infections may occur. It is possible for this organism to gain entrance to the body if there is a relaxation of aseptic precautions.

REFERENCES

ABEL, A. LAWRENCE (1957), *Proc. roy. Soc. Med.*, vol. 50, page 135.

ALLEN, A. W. (1953), *Surg. Gynec. Obstet.*, vol. 96, page 107.

BARKER, N. W., NYGARRA, K. K., WALTMAN, W., and PRIESTLEY, J. T. A. (1940), *Proc. Mayo Clin.*, vol. 15, page 769.

BELL, G. O., SWINTON, N. W., and HURXTHAL, L. M. (1957), *Surg. Clin. N. Amer.*, June, page 737.

BUCKWALTER, J. A., SHROPSHIRE, R., and JOINER, B. A. (1955), *Surg. Gynec. Obstet.*, vol. 101, page 483.

CASWELL, H. T., SCHRECK, X. M., BURNETT, W. E., CARRINGTON, E. R., LEARNER, N., STEEL, H. H., TYSON, R. R., and WRIGHT, W. C. (1958), *Surg. Gynec. Obstet.*, vol. 106, page 1.

CUTHBERTSON, ALAN, and MARSHALL, D. (1958), in the press.

DE LAUGHTER, G. D., and ANLYAN, W. G. (1956), *Surg. Gynec. Obstet.*, vol. 103, page 695.

EVANS, A. D., and EVANS, M. (1956), *Lancet*, vol. i, page 771.

GIBBS, N. M. (1957), *Brit. J. Surg.*, vol. 45, page 209.

GOBLE, A., and HUGHES, E. S. R. (1958), in the press.

GOLIGHER, J. C. (1958), *Ann. roy. Coll. Surg. Engl.*, vol. 22, page 311.

GOLIGHER, J. C., LLOYD-DAVIES, O. V., and ROBERTSON, C. T. (1951) *Brit. J. Surg.*, vol. 38, page 467.

GRESHAM, G. A., and GLEESON-WHITE, M. H. (1957), *Lancet*, vol. i, page 651.

HAUSMANN, W., and KARLISH, A. J. (1956), *Brit. med. J.*, vol. ii, page 845.

HUGHES, E. S. R. (1958), in the press.

KISTNER, R. W., and SMITH, G. V. (1954), *Surg. Gynec. Obstet.*, vol. 98, page 437.

LEITHAUSER, D. J. (1958), *Surg. Gynec. Obstet.*, vol. 106, page 100.

PATERSON, J. C., and MCLACHLIN, JOHN (1954), *Surg. Gynec. Obstet.*, vol. 98, page 96.

POSTLETHWAITE, R. W., ADAMSON, J. E., and HART, D. (1958), *Surg. Gynec. Obstet.*, vol. 106, page 257.

ROSSLE, R. (1937), *Virchows Arch. path. Anat.*, vol. 300, page 180.

WILSON, PATRICIA (1956), *Med. J. Aust.*, vol. 2, page 289.

THROMBOSIS

By V. J. McGovern

Fairfax Institute of Pathology, Royal Prince Alfred Hospital, Sydney

WHILE there have been many studies of blood coagulation and of the haemodynamics involved in thrombosis, there seems to be a widespread reluctance to devote time to the study of endothelium even though it is the failure of vascular endothelium to maintain its anticoagulant properties that is the eventual cause of thrombosis.

In this paper I intend to describe the mechanism by which an anticoagulant lining is maintained in blood vessels and to discuss the ways in which it may be disturbed.

Normal Endothelium

Normal endothelium can be shown in tissue spreads of vascular intima to be composed of flattened cells separated by argyrophilic cement lines. More intense silver staining shows that there is also an argyrophilic surface film covering the endothelial cells. This film is thinnest where it overlies the projecting cell muclei and thickest where adjacent cells meet. Gentle scraping of the surface of the fixed preparation removes not only the surface film but also the intercellular lines leaving behind the naked endothelial cells (Figs. I and II). Touching the unfixed endothelial surface of living tissues removes the cement whereupon the underlying cells assume a fusiform shape.

These features have led to the concept that the endothelial cells secrete around themselves a semi-diffluent gelatinous material which acts as a limiting membrane. The film merges at the line of contact of contiguous cells, forming the intercellular cement lines and also a continuous surface pellicle. From other observations it appears that endothelium is continuously manufacturing this cement substance which is just as continuously being washed away in the circulation (McGovern, 1955, 1956a).

Various substances are soluble in the endothelial cement. Heparin is one of these, and this fact was used by Samuels and Webster (1952) in a method for staining the intercellular lines. Heparin comes from mast cells (Jorpes, 1946) which secrete in addition, histamine (Riley, 1953) and a third substance capable of altering the consistency of cement and thereby its permeability (McGovern, 1956a).

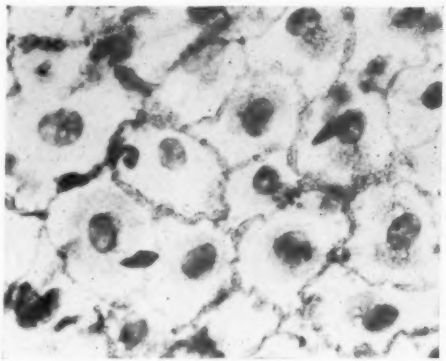


FIG. I. Normal area of vascular endothelium from human mitral valve of male aged 55 years, dying from myocardial infarction. Silver nitrate and thionin (x 640).

Relationship of Mast Cells to Endothelial Surface

Certain vessels contain mast cells in their intimal coat immediately beneath the endothelial cell layer. The aorta is one of these and in its intima mast cells average more than 300 per square millimetre of endothelial surface. The branches of the aorta such as the coeliac axis, the renal and mesenteric arteries do not usually contain mast cells beyond their origins. Mast cells are present in the intima of the carotid arteries but do not continue into the cranial cavity. Below the inguinal ligament mast cells are uncommon though they are sometimes found as far as the popliteal artery. The coronary arteries contain

* Based upon a contribution to a symposium held by the Royal Australasian College of Surgeons in Sydney on 25 June, 1958.

between 100 and 150 intimal mast cells per square millimetre of endothelial surface, and in the pulmonary arteries they number between 100 and 200 (Fig. III).

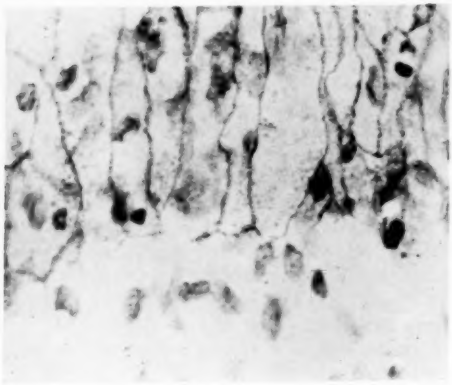


FIG. II. Aortic endothelium from female aged 53 years showing an area from which the cement film was accidentally removed after fixation and staining. The cytoplasm of endothelial cells does not stain and only the bare nuclei are discernible. Silver nitrate and thionin (x 500).

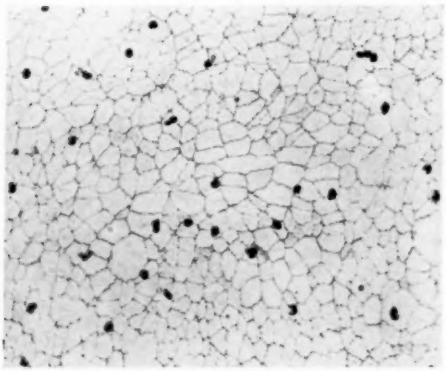


FIG. III. Aortic intima from child aged 4 years with congenital heart disease, showing the intimal mast cells. Silver nitrate and thionin (x 150).

Veins, apart from the venae cavae, seldom contain intimal mast cells, but most vessels contain mast cells in their adventitiae. The cerebral vessels however, are exceptions; there are no mast cells in the leptomeninges or within the brain substance.

FUNCTIONS OF MAST CELLS

The importance of mast cells is in their secretions. In the aorta, coronary and pulmonary arteries, mast cell secretions liberated in the intima seep through the endothelial cement lines dissolving in them and in the surface cement film. When mast cells secrete to excess their granules become depleted and metachromatic bubbles can then be demonstrated in the cement lines. Furthermore streamlines of metachromatic material may be found in the cement of distant vessels such as the basilar artery which have no intimal mast cells (Figs. IV and V). It appears that excess secretion from aortic mast cells is trapped from the circulation by the cement of vessels which have no intimal mast cells. This is probably facilitated by that mast cell secretion which alters the consistency of endothelial cement so that streamlines are formed. The metachromatic reaction to basic stains such as thionin which is exhibited by the stream lines is attributed to heparin.

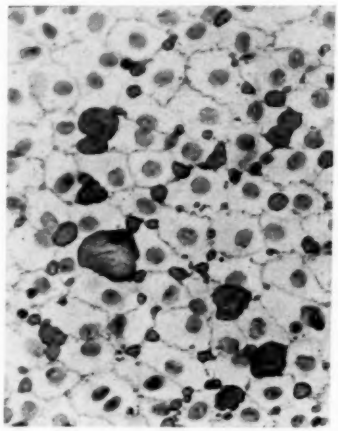


FIG. IV. Aortic intima from male aged 41 years dying from myocardial infarct. The metachromatic bubbles in the cement lines are thought to be derived from the subjacent mast cells which have been completely exhausted, being represented only by the small dark nuclei. Silver nitrate and thionin (x 300).

From these observations it is inferred that mast cells in the aortic intima are chiefly responsible for the anticoagulant property of the lining of arterial vessels in general. In the case of veins, mast cell secretions must be chiefly derived from the regions of the vasa venorum in the adventitiae and from cells related to capillaries in the skin and integumentary tissues.

REACTION TO INJURY OF VASCULAR ENDOTHELIUM

Experimentally, injury causes rat's vascular endothelium to produce increased amounts of cement. If the noxious agent affects mast cells also, metachromatic material is liberated which percolates through the intercellular cement lines and dissolves in the new cement which then spreads over the irritated surface (McGovern, 1955).

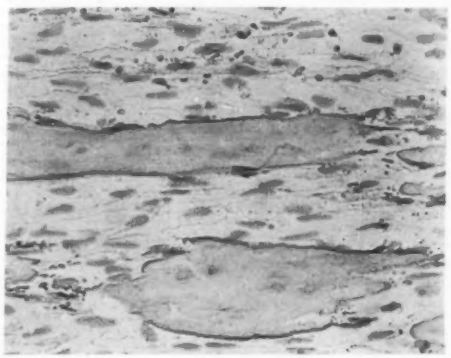


FIG. V. Basilar artery from male aged 66 years dying from carcinoma of pancreas. Stream lines of metachromatic material cover the endothelium. Silver nitrate and thionin (x 150).

In human vessels, both arteries and veins, particularly in the elderly, one frequently sees the reaction to injury identical with that experimentally produced in the rat. The pattern of the metachromatic cement film in the human is usually in the form of streamlines (Figs. V and VI). In veins the metachromasia, and therefore the heparin concentration, is weaker than in arteries, due no doubt to the less direct route by which heparin gets into veins. Arterial heparin is mainly derived from the aorta while in veins the secretions of adventitial mast cells, passing via the vasa venorum, reinforce whatever residual quantity of heparin there is of aortic origin.

One must conclude from these observations that injurious substances get into the circulation from time to time and excite the reaction to injury.

FAILURE OF THE REACTION TO INJURY

If the reaction to injury fails, thrombosis results. Experimentally, thrombosis is liable to occur if an injury is so severe that it impairs the ability of endothelium to produce enough cement to replace that which is washed away in the bloodstream. One must recollect, too, that cement is the vehicle for heparin. Furthermore, interference with the activity of mast cells by depleting them, neutralizing their secretions or hindering the passage of their secretions into vessels also predisposes to thrombosis. Let us briefly consider some of the factors which experimentally have been found to affect the reaction to injury and predispose to thrombosis.

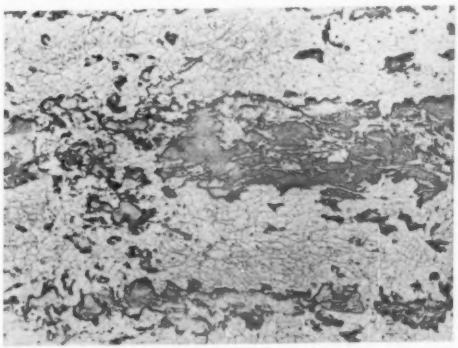


FIG. VI. Stream lines of coalescing metachromatic material dissolving in cement covering endothelium of mitral valve in male aged 49 years dying from pneumonia. Silver nitrate and thionin (x 75).

(*a*) *Corticoids*

In the rat, mast cell activity is decreased by cortisone. Prolonged administration causes reduction in the size of mast cells and slows up their ability to replenish their stores of secretion after they have been depleted. Halpern (1956) found that cortisone markedly reduces the rate of histamine resynthesis. Similarly I have found that in cortisone treated animals there is a deficiency of heparin and also of the secretion which alters the consistency of cement. Injury to vessels is then more likely to cause thrombosis than in normal animals. Whereas excessive stimulation of mast cells is usually followed by their multiplication, there is no increase in their numbers while cortisone is being administered.

(b) Antihistaminics

The antihistamine drugs diminish vascular permeability by toughening the endothelial cement (McGovern 1956b). The reduction in permeability affects the passage of mast cell secretions into vessels as well as the passage of fluids outwards so that less heparin is carried in the blood stream to sites where it is required. Chlorpromazine is an antihistaminic as well as a sedative and it, too, diminishes vascular permeability. This must have contributed to the very high incidence of thrombosis and embolism found when the drug was used in the production of artificial hibernation by Laborit and Huguenard (1954). Slowing the circulation was possibly a further contributory factor in those cases.

(c) Cell nuclear derivatives

From normal cell nuclei Archer (1958) has obtained extracts which deplete mast cells and neutralize heparin. I have found that although these substances do not injure endothelium in any way, even small amounts allow thrombosis to be produced by injuries which would ordinarily be effectively countered by the reaction to injury. The responsible agents are probably histones, i.e., basic amines which are normally present in cell nuclei. One can readily imagine conditions of cell destruction in which dangerous quantities of these substances are liberated into the circulation.

(d) Stasis

Slowing the circulation through the rat's femoral vein does not cause thrombosis even when combined with mast cell depletion or the local neutralization of heparin. Thrombosis of the femoral vein is, however, much more readily produced by slight injury when the circulation is slowed.

Under experimental conditions injury to endothelium is necessary for the production of thrombosis.

INCIDENCE OF THROMBOSIS

At Royal Prince Alfred Hospital in the past eight years pulmonary embolus of sufficient magnitude to cause sudden death was encountered at autopsy 73 times. In addition pulmonary infarction of a degree which contributed towards death of the patient was found on 25 occasions. While extensive search for thromboses in the lower limbs has not been routine, there were 67 examples of thrombosed femoral vessels unaccompanied by pulmonary embolus or infarction. There were thus 165 examples of venous thrombosis in 3,185 autopsies from the general hospital, an incidence of 5 per cent. while massive pulmonary embolus had an incidence of 2.3 per cent. As in other published series, medical cases predominated and cardiovascular disorders formed the greatest proportion.

TABLE 1

THROMBOSIS AND EMBOLISM

	Post-operative	*No operation*	*Totals*
Hypertensive and ischaemic cardiovascular disease	13	53	66 (40 per cent.)
Rheumatic heart disease		20	20 (12 per cent.)
Malignant disease	20	28	48 (29 per cent.)
Miscellaneous	18	13	31 (19 per cent.)
Total:	51	114	165

(a) Hypertension cardiovascular disease

Hypertension accelerates and intensifies the atherosclerotic process and most of the subjects in this category had some degree of heart failure due to myocardial ischaemia. In many there had been myocardial infarcts, recent in some, healed in others. In these the slowing of the circulation seems to have been the

factor predisposing to thrombosis and possibly the neutralization of heparin by the products of nuclear dissolution in cases of myocardial infarction played an accessory part.

(b) *Rheumatic heart disease*

Patients with chronic rheumatic heart disease are unusually liable to suffer thromboses (McGovern, 1953) and reference to Table I will indicate the high proportion they comprise. Whereas it is the slow circulation of failure that predisposes to thrombosis in hypertensive cardiovascular disease, there is usually in chronic rheumatic heart disease a hypodynamic circulatory state in the lower limbs even when there is no heart failure, and this seems to be the reason for the variety of thromboses and emboli found in this disorder.

There is no doubt that slowing the circulation is an important precipitating cause of thrombosis. Some patients spend almost a lifetime in bed yet never develop thrombosis while others sitting still for an hour or two in front of a television screen do so. When slowing of the circulation for such short periods is followed by thrombosis, other predisposing factors must also have been present. As I have already mentioned, I have not been able to produce thrombosis in the rat's femoral vein merely by slowing the circulation. There must be injury as well.

If the findings in animal experiments are applicable to humans, then the inference is that in these cases there is already some injury to the endothelium which is likely to be followed by thrombosis when the circulation is slowed.

(c) *Malignant disease*

Malignant disease whether carcinoma or sarcoma is frequently accompanied by thromboses, and pulmonary embolus is one of the commonest modes of death. Migrating phlebitis although a rare condition sometimes accompanies malignant disease, clearing up when the cancer is extirpated only to recur if metastases develop.

Carcinoma of the body or tail of the pancreas is generally regarded as being the commonest neoplasm to be associated with thromboses, but cancers of the lung and cancers of the alimentary tract are each numerically more frequent.

The factor responsible for the development of thromboses in cancer is not known as the ordinary measurable components of the blood are normal.

The most likely explanation is that basic amines liberated from degenerating cancer cells neutralize the heparin dissolved in the endothelial cement and so augment any tendency to thrombosis that already exists. Moore *et alii* (1957), examining the blood from the peripheral circulation have shown that carcinoma cells can be demonstrated in more than half their cases. Yet only an occasional cell gives rise to a metastasis so that destruction of the remainder must set free some of the basic amines which antagonize the action of heparin.

(d) *Miscellaneous*

This group includes patients undergoing operations of election such as gastrectomy for peptic ulcer, acute abdominal disorders such as pancreatitis and intestinal obstruction and infections such as pneumonia.

The precipitating cause is not clear. One can only guess that the stasis involved in bed rest has played some part.

CORRELATION

Experimentally I have found that stasis alone does not cause thrombosis nor does depletion of mast cells or neutralization of available heparin by protamine or other substances. Thrombosis can only be produced by injury to vascular endothelium although these other manoeuvres do facilitate the process in what would otherwise be a subliminal injury.

The conclusions reached through animal experiments seem to have valid application in the problem of thrombosis in humans; that stasis and heparin depletion lead to thrombosis only when there is already an injury. The nature of the injurious agent remains to be discovered.

ACKNOWLEDGEMENTS

A good deal of the experimental work quoted in this paper was performed in the Department of Morbid Anatomy, University College Hospital Medical School, London, under Professor Sir Roy Cameron, F.R.S. The photomicrographs were made by the Department of Illustration, University of Sydney.

REFERENCES

ARCHER, G. T. (1958), *Nature*, vol. 182, page 726.

HALPERN, B. N. (1956), in "Ciba Foundation Symposium on Histamine," London.

JORPES, J. E. (1946), "Heparin in the Treatment of Thrombosis." 2nd Edition, London.

LABORIT, H., and HUGUENARD, P. (1954), quoted by J. Adams-Ray in "Thrombosis and Embolism, an International Symposium". Basle, 1955.

MCGOVERN, V. J. (1953), *Aust. Ann. Med.*, vol. 2, page 81.

——, (1955), *J. Path. Bact.*, vol. 69, page 283.

——, (1956a), *J. Path. Bact.*, vol. 71, page 1.

——, (1956b), *J. Path. Bact.*, vol. 72, page 143.

MOORE, G. E., SANDBERG, A., SCHUBARG, J. K. (1957), *Ann. Surg.*, vol. 146, page 580.

RILEY, J. F. (1953), *J. Path. Bact.*, vol. 65, page 471.

SAMUELS, P. B., and WEBSTER, D. R. (1952), *Ann. Surg.*, vol. 136, page 422.

BLOOD VOLUME STUDIES IN AGED MEN*

By T. S. Reeve, T. H. Oddie, Sheilah Bowman and F. F. Rundle

Unit of Clinical Investigation, The Royal North Shore Hospital of Sydney

Introduction

During the past several decades, the frequency and magnitude of surgical operations being done on old people have steadily increased. In particular, the scope of extirpative surgery for cancer has widened immeasurably. Low mortality and morbidity rates can only be achieved if the circulating blood volume, and especially the red-cell mass, are well maintained, the red cells being required to transport oxygen vital to the function of the ageing cells of the myocardium, brain and kidney.

The blood volume in later life has been studied before. Gibson and Evans (1937) suggested that the blood volume decreased with advancing age. Perry *et alii* (1956) calculated a nomogram for red cell mass and similarly found that people in older age groups fell short of normal blood volume by 10 per cent. On the other hand, Cohn and Shock (1949) and Schmidt *et alii* (1956) found no significant change in total blood volume, although the latter workers found a small but significant diminution in the red cell volume, of their aged subjects. Also, Beling *et alii* (1952) suggested that a level of 85 ml. of circulating blood per kilogram of body weight was the optimal value for the circulating blood in old subjects; this figure is high compared with the values obtained in young people.

In view of this lack of agreement, it was decided to undertake a review of geriatric males in Sydney, in an endeavour to determine the general level of the blood volume in this section of the community.

Material

Ninety-seven aged men, inmates of a geriatric hospital, volunteered for blood volume determinations. They fell into categories with diseases common to older age groups, and frequently encountered by surgeons. There were patients with hypertension, or other controlled heart disease, those convalescent from cerebro-vascular accidents, those with coronary insufficiency, some with enlarged prostates, some that were senile and a small number convalescent from surgery or pneumonia. Their ages lay between 55 and 89 years, and the distribution is recorded in Table I. The average age of the 97 patients was seventy-six years. Despite their geriatric conditions, the great majority were active and ambulatory and represented a background on which malignant disease commonly occurs.

The weight and height of each subject were determined, and from these his surface area was derived, using the nomogram of Talbot *et alii* (1952).

Table 1

AGE DISTRIBUTION OF MALES WHOSE BLOOD VOLUME WAS DETERMINED IN A HOSPITAL FOR AGED MALES

Age in Years	*Number of Subjects*	*Per cent. of Total*
55 - 59	8	8.25
60 - 69	26	26.81
70 - 79	48	49.48
80 - 89	15	15.46
	97	100.00

Method

Blood volumes have been carried out by the method of Meyer (1956) with some modifications. The method depends on the affinity of radio-active chromium in its tetravalent form ($Na_2 Cr^{51} O_4$), for the globin fraction of haemoglobin. This affinity was demonstrated by Gray and Stirling (1950) who first described blood volume determinations with Cr^{51}.

*This work was supported by a grant-in-aid from the New South Wales State Cancer Council.

The method makes use of banked blood. Seventy-five millilitres of group O, Rh negative blood, with A.C.D. anticoagulant, are collected from the blood bank and to this volume is added 450μc of Cr^{51}. This solution is gently rotated several times and then placed in a water bath and incubated at 37° C. for one hour. Fifteen ml. of normal saline are then added to the solution, together with 75 mg. of ascorbic acid, which being a powerful reducing agent prevents further uptake of Cr^{51} by the erythrocytes. The solution is then gently rotated in a circular fashion for ten minutes to ensure complete mixing.

Ten ml. aliquots of this solution are drawn up with accurately calibrated syringes, and this volume of "tagged" blood is then injected into an arm vein. The other arm is used for withdrawing subsequent samples, the first sample being taken twenty minutes after the initial injection. This interval allows mixing of the "tagged" material with the entire circulating blood volume. The tourniquet is released once the sampling syringe is in the vein, so that the blood withdrawn is a freely flowing venous sample, not a pooled one. The sample withdrawn is transferred to a tube containing 0.2 ml. of 20 per cent. potassium oxalate in the dried state.

PREPARATION OF ALIQUOTS FOR COUNTING

(a) *Standard*

One ml. of the stock solution of "tagged" blood is placed in each of three 50 ml. volumetric flasks, and 49 ml. of water are added to each. After haemolysis occurs a 4 ml. sample from each is transferred to a plastic assay vial for counting.

Ten ml. of the injection material is centrifuged for five minutes at 4,000 revolutions per minute, and 1 ml. of the supernatant plasma is transferred to each of three plastic assay vials, and 3 ml. of water are added to each.

Three separate haematocrit determinations are made of the injection material, the samples being centrifuged for thirty minutes at 3,000 revolutions per minute. A correction is applied to the red cell column to compensate for trapped plasma (Chaplin and Mollison, 1952).

(b) *Blood from each patient*

One ml. of well mixed whole blood withdrawn from the patient is placed in each of three plastic assay vials, and 3 ml. of water are added to each. The vials are capped and allowed to haemolyse for one hour. Supernatant samples are prepared as already described and the haematocrit values are determined, an extra corrective factor being introduced in the patient's haematocrits. The factor 0.91 (Chaplin and Mollison, 1953) is used to convert the haematocrit to whole body haematocrit, the correction for trapped plasma is made as before.

(c) *Counting*

A well-type scintillation counter is used, and the various samples are counted for the following times:

Background—eight minutes.

3 injection samples—two minutes each.

2 injection supernatant samples—one minute each.

3 patient whole blood samples—fifteen minutes each.

3 patient supernatant samples—two minutes each.

Background—eight minutes.

The same routine is followed for any number of patients.

(d) *Calculations*

Let, B counts/minute = the mean net counting rate (i.e. after subtraction of background) for the whole blood injection samples.

S counts/minute = the mean net rate for the supernatant injection samples.

h = the haematocrit of this material, corrected for trapped plasma.

Similarly let B_A, S_A, and h_A = the corresponding values for patient A.

The whole blood volume V_A for patient A is derived from

$$V_A = \frac{125\,B - 10S\,(1 - {}^{h}/_{100})}{B_A - S_A\,(1 - {}^{h}A/_{100})} \text{ml.} \quad (1)$$

Similarly the red cell volume v_A

$$v_A = {}^{h}A\ V_A/100 \quad \text{ml.} \quad (2)$$

To ensure general uniformity of results all determinations were carried out by two people, the one (T.R.) injecting and withdrawing all samples, the other (S.B.) carrying out the technical preparation for counting, and doing the counts and calculations.

Fig. II records the red cell volume per kilogram in the aged male patients, with the mean value represented by a continuous line, and similarly the value recorded by De Gruchy as an interrupted line. The individual values are recorded along a weight ordinate

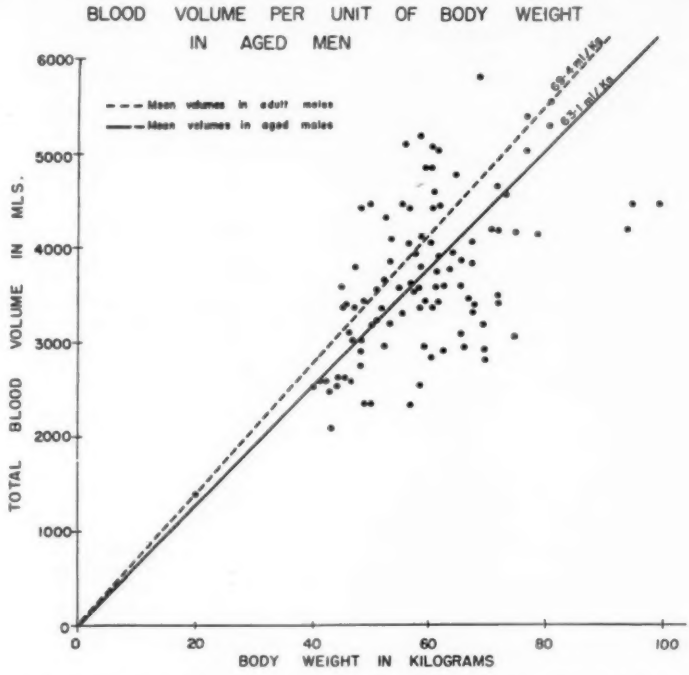


FIG. I. The blood volumes of the aged male subjects is shown plotted against body weight. The continuous line represents the mean value. The broken line has been arbitrarily drawn to represent the mean value in adult males reported by Crawford and De Gruchy (1958).

RESULTS

The results of our determinations are shown in Table 2. They may first be compared with those of other workers, who used younger people as subjects. Crawford and De Gruchy (1958) recorded results of total blood and red cell volumes determined with blood volumes of the aged subjects in this Cr^{51} in Australian adult males. In Fig. I, the study are plotted against the body weight in kilograms. A continuous line has been drawn to represent the mean value, while a broken line has been arbitrarily drawn to represent the mean value reported by Crawford and De Gruchy (1958).

to give adequate scatter of the points. It can readily be seen that there is a difference of 6.3 ml./kg. in the total blood volume, and 6.1 ml./kg. in the red cell volume between the geriatric and young males. This difference between old and young males, it may be emphasized, is almost entirely due to the difference between their red cell volumes.

Baker, *et alii* (1957), using I^{131} serum albumin, established a figure for the blood volume per square metre of surface area, in a group of normal hospital patients. In Fig. III our blood volumes of aged men are plotted against body surface area, and a continuous line represents the mean value. An interrupted line has been drawn to show Baker's mean

result. The blood volume of our aged men is again noted to be deficient in comparison to a "normal" group. The difference between these values is significant on statistical examination ($p < 0.001$).

gram with a mean value of 63.1 ml. per kilogram. These figures are well below those of Beling and his co-workers, who advocated an optimal level of 85 ml. of whole blood per kilogram of body weight in the aged. Their

TABLE 2

BLOOD VOLUME DETERMINATIONS IN 97 GERIATRIC PATIENTS

	TOTAL BLOOD VOLUME			RED CELL VOLUME		
	Mean	*Standard Deviation*	*Standard Deviation of Mean*	*Mean*	*Standard Deviation*	*Standard Deviation of Mean*
ml. per Kg. body weight	63.1	±12.7	±1.3	21.60	±4.7	±0.48
litres per sq. metre surface area	2.220	± 0.412	±0.042	0.770	±0.169	±0.017

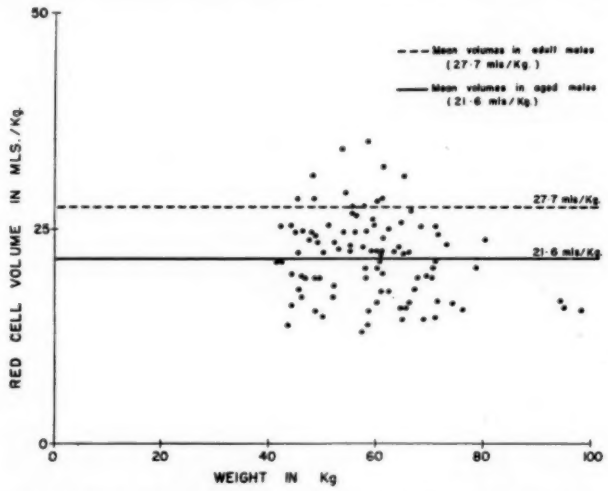


FIG. II. The red cell volume per kilogram of aged males is plotted against the body weight in kilograms. The mean value is represented by a solid line. The broken line represents the value recorded by Crawford and De Gruchy (1958) for adult males.

Finally the red cell volume was plotted against body surface area (Fig. IV) and compared with the mean figure of Gibson and Evans (1937), who used Evans blue dye (T 1824) in their determinations. The figures again point to a significantly reduced red cell volume in the aged group studied.

Discussion of results

The range of blood volume in the aged group under study was 42.6-91.8 ml. per kilo-

figure would appear to be high when compared with values obtained by other workers both in "normal" hospital populations (Whyte, 1958; Baker, 1957; Crawford and De Gruchy, 1958; Reeve and Veall, 1949) and in the aged as determined by Schmidt *et alii* (1956), Perry *et alii* (1956), and ourselves.

As Whyte (1958) has aptly pointed out, the attempt to establish "normal" values of blood

volume in relation to body weight only is unsound. Body composition, with respect to the muscle and the poorly vascularized fat compartments, varies and their relative proportions significantly affect the blood volume. A number of formulae have been advocated (Whyte, 1956, and Allen, 1956), to allow for these factors. Expressing blood and red cell volumes in terms of body surface area minimizes the variation due to relatively avascular fat.

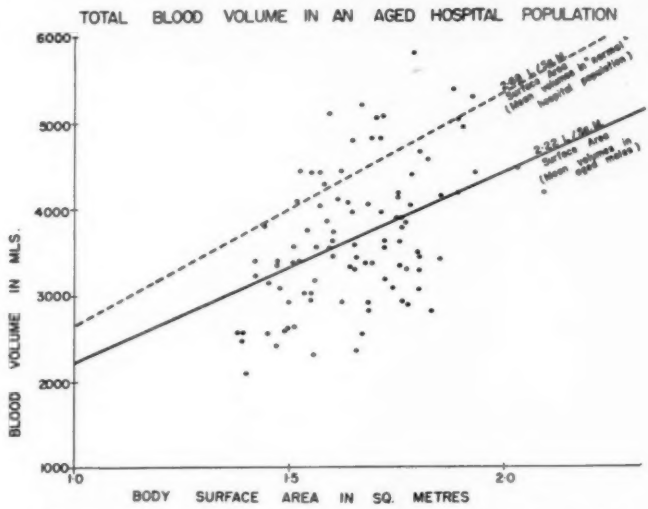


FIG. III. The blood volume in aged men is plotted against the body surface area, the solid line being the mean value. The interrupted line represents the mean value determined by Baker *et alii* (1957) for a normal hospital population.

On this basis the aged males were still found to be deficient in total volume and reduction in red cell volume was very largely responsible for the deficiency. The total blood volume of the aged men was found to be 80 per cent. of the "normal" figures and the red cell volume, 65 per cent. of the "normal" values obtained by Crawford and De Gruchy (1958). These decreases in red cell volume and total blood volume are statistically significant. However, in the widely varying values obtained in our group, an upward trend in blood volume was noted both with increase in weight and increase in surface area.

The values in our group are lower than those in an aged group studied by Schmidt *et alii* (1956), who found the total blood volume to be 71.3 ml. per kilogram (range 53.4-88.7 ml. per kilogram), and 2.70 litres per square metre of body surface area, and the red cell volume to be 1.08 litres per square metre. They used Evans blue and found an overall reduction of 8.5 per cent. in red cell volume and of 3.2 per cent. in plasma volume as compared with the mean values for normal subjects studied by Gibson and Evans. The patients studied by Schmidt *et alii* (1956) were in a State hospital under custodial care. The discrepancy in total volumes between our results and those of Schmidt *et alii* (1956) would be accounted for in part by the use of Evans blue dye, but the difference in red cell volume could not be so explained. The general level of nutrition in their series may have been better, the patients having lived under supervision for many years. Many of our subjects were short stay patients in the hospital and had previously lived alone. They were possibly malnourished. Nevertheless, it is patients such as these that we are frequently called upon to treat surgically.

It may be concluded that the total blood volume and especially the red cell mass are significantly reduced in geriatric subjects. This must make them vulnerable to relatively minor degrees of blood loss. They are indeed doubly vulnerable because of the dependence of ageing cells in the heart, brain

and kidneys on uninterrupted oxygen transport.

Clearly the blood loss associated with major excisional surgery, as in cancer, must be made good as it occurs. Because of the wide inter-individual variations found, the ideal is to measure the blood volume of each elderly patient undergoing such surgery. The red cell mass should then be maintained, during and after surgery, at the patient's usual level. Failure to observe this precaution may account for at least part of the increased mortality and morbidity associated with surgery in the elderly.

if deficient should be brought up to an approximately normal value for the patient's age and carefully maintained during and after operation.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the courtesy of the Director-General of Health, N.S.W., and Dr. G. S. Procopis in allowing free access to geriatric patients in Lidcombe State Hospital and Home.

Also greatly appreciated was the willing co-operation of Dr. W. Hobart, the ward sisters and patients, without whose help the study could never have been completed. The radio-active chromium was supplied by the Commonwealth Department of Health.

The blood for "tagging" was supplied by the Blood Bank of the New South Wales Division of the Red Cross Society.

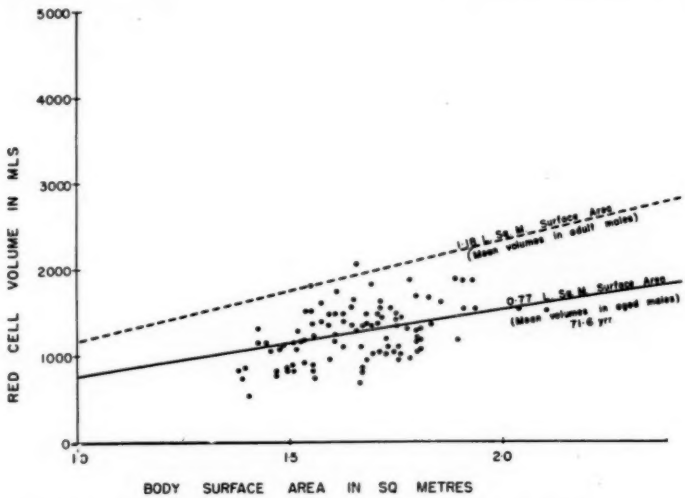


FIG. IV. The red cell volume of aged men is plotted against the body surface area. The mean value is shown as a solid line. The broken line represents mean value in elderly males as recorded by Gibson and Evans (1937).

SUMMARY

1. Using the isotope Cr^{51}, the red cell and total blood volumes have been determined in a group of 97 men aged from 55 to 89 years. A description of the method is given.
2. The total blood volume of these geriatric patients was found to be systematically reduced both in relation to body weight and to body surface area. The total blood volume deficit was chiefly dependent on a reduction of the red cell mass.
3. Determination of the blood volume is advocated in all aged patients who are to undergo major surgery. The red cell mass

REFERENCES

ALLEN, T. H., PENG, M. T., CHEN, K. P., HUANG, T. F., CHANG, C., FANG, H. S. (1956), *Metabolism*, vol. 5, page 328.

BAKER, R. J., KOZOLL, D. D., MEYER, K. A. (1957), *Surg. Gynec. Obstet.*, vol. 104, page 183.

BELING, C. A., BOSCH, D. T., CARTER, O. B., Jr. (1952), *Geriatrics*, vol. 7, page 179. (Quoted from Schmidt *et alii* 1956.)

CHAPLIN, H., MOLLISON, P. L. (1952), Blood, vol. 7, page 1227.

——, —— (1953), *J. clin. Invest.*, vol. 32, page 1309.

COHN, J. E., SHOCK, N. W. (1949), *Amer. J. med. Sci.*, vol. 217, page 388.

CRAWFORD, H., DE GRUCHY, G. C. (1958), *Med. J. Aust.*, vol. 1, page 657.

GIBSON, J. G. 2nd.; EVANS, W. A., Jr. (1937), *J. clin. Invest.*, vol. 16, page 317.

GRAY, S. J., STERLING, K. (1950), *Science*, vol. 112, page 179.

——, —— (1950), *J. clin. Invest.*, vol 29, page 1604.

MEYER, L. M. (1956), *J. Amer. med. Ass.*, vol. 160, page 1312.

PERRY, F. A., RANDALL, H. T., POPPELL, J. W., ROBERTS, K. E. (1956), *Surg. Clin. N. Amer.*, vol. 1, pages 301-313.

REEVE, E. B., VEALL, N. (1949), *J. Physiol.*, vol. 108, page 12.

SCHMIDT, L. A., 3rd; JOB, V., FLOTTE, C. T., HODGSON, P., MCMATH, M. (1956), *Surgery*, vol. 40, page 938.

TALBOT, N. B., SOBEL, E. H., MCARTHUR, J. W., CRAWFORD, J. D. (1952), "Functional Endocrinology from Birth Through Adolescence," Cambridge, Mass., Harvard University Press.

WHYTE, H. M. (1956), *Aust. Ann. Med.*, vol. 5, page 192.

—— (1958), *Med. J. Aust.*, vol. 1, page 802.

THE ADMINISTRATION OF PRESUREN

By T. R. Morley

Perth

THE free use of steroids in anaesthesia using 21-hydroxy-pregnane-3, 20-dione sodium succinate has been hampered by the various controversial methods put forward as to the best method of administration.

To date, this agent has almost invariably been administered in a dilute solution necessitating the intravenous infusion of as much as 1 litre of fluid for induction of anaesthesia, and requiring a waiting period of ten minutes or longer before the administration of other anaesthetic or analgesic agents is commenced. The supplementing of the steroid by the administration of intravenous pethidine or Omnopon or the inhalation of ether, trichlorethylene or cyclopropane has been recommended and, in some cases, it has been advocated that the ideal is to induce anaesthesia with thiopentone and then follow this by the administration of a steroid.

During the past year Presuren was administered to 289 cases in association with Dr. Hudson and the anaesthetic staff of the Royal Perth Hospital using previously accepted and other techniques and, as a result, I came to the conclusion that insufficient use was being made of the potentiation of the anaesthetic and analgesic properties of nitrous oxide when used with the steroids. Further, with the introduction of Presuren, and following the work done by Stedtfeld (1957) on the administration of this agent in warm solution it was possible to eliminate the cumbersome technique of administering large volumes of dilute solution.

Properties of Presuren

Presuren is 21 hydroxy-pregnane-3,20-dione which has been rendered water soluble by means of esterification with succinic acid, the product used being the sodium hemisuccinate. It is a white powder presented in 1 G. and 0.5 G. bottles, easily soluble in warm normal saline and is administered intravenously in 2½ per cent. or 5 per cent. solution.

It has no oestrogenic, androgenic or other specialized hormonal activity associated with certain other steroids and does not cause water or salt retention. Its potency is less than that of thiopentone but it has a higher therapeutic index and three times the margin of safety.

The rapid administration intravenously of 0.5 to 1 G. will result in the patient falling asleep in five to ten minutes and with the smaller dose no respiratory depression occurs.

Provided the Presuren is administered rapidly and in a warm solution using normal saline as the solvent thromboses do not occur.

Thiopentone, gallamine, atropine, neostigmine and methylamphetamine are miscible with Presuren. Pethidine, d-tubocurarine and suxamethonium are not.

Administration

Premedication is with Omnopon and atropine or pethidine and atropine given one hour pre-operatively but in obstetric and neurosurgical cases, or where any respiratory obstruction is present, only atropine is given.

A 20 mil. ampoule of normal saline is placed in water at a temperature of between 60 and 65 degrees Centigrade and left while an 18 gauge Mitchell or other needle of the self sealing type is inserted into a large vein at the antecubital fossa. In abdominal and thoracic cases a second needle is inserted into another vein, usually on the back of the hand. No drugs, other than Presuren and procaine are administered through the Mitchell needle.

One gram of Presuren is then dissolved in the warm normal saline and the resulting solution tested on the back of the hand. When it can be tolerated without discomfort the solution is injected rapidly, taking not longer than five or ten seconds, into the vein at the antecubital fossa and this is immediately followed by the slow injection, through the same needle, of 5 mils. of 1 per cent. procaine. Alternatively the procaine may be added to the solution of Presuren.

Without waiting for the patient to fall asleep the administration of nitrous oxide 6 litre flow and oxygen 2 litre flow is commenced. Within four or five minutes the patient is asleep and automatic respiration is established. At this stage, unless the trachea is to be intubated, the preparation of the patient may be commenced and the operation started.

Soon after automatic respiration is established there is a short period of hyperpnoea followed by reduction in tidal volume progressing in some cases to apnoea. At this stage, if so desired, intubation may be performed with ease without relaxants. The vocal cords will still move if directly stimulated but intubation is easy and bucking on the tube does not occur.

Respiration is then assisted or controlled for a few minutes and tidal volume soon returns to its normal level. At this stage the cuff on an endotracheal tube may be inflated, the flow rates are reduced to 3 to 1 and this is maintained throughout the operation.

With these doses and flow rates the average duration of anaesthesia, during which an endotracheal tube is tolerated without either local analgesia or the addition of relaxant drugs is one and one half hours.

No supplements such as pethidine, Omnopon or other analgesic or anaesthetic drugs, or relaxants are given except in abdominal surgery when relaxants must usually be given, but, in reduced doses, to ensure adequate relaxation.

Although control of respiration may be taken over with ease at any time during anaesthesia relaxant should be given for surgery within the pleural cavity.

Lightening of anaesthesia is indicated by slight movements of the patient, rise in blood pressure or tachypnoea and in such cases a further dose of 0.5 G. of 2½ per cent. or 5 per cent. solution of warm Presuren, again followed by 5 mils. of 1 per cent. procaine, should be given. Such supplements usually last for one hour.

The initial dose of Presuren usually lasts for one and one half hours but the duration varies with the age and condition of the patient and in many old and bad risk cases it was found that the duration of a single dose of less than 1 G. was considerably longer than average. At the beginning of this series it was my practice to give a small initial dose in the above type of patient and to supplement it later. Now, provided the operation is likely to last longer than one and one half hours, I tend to give an initial dose of 0.75 G. to 1 G. and by obtaining a longer period of anaesthesia avoid supplementary doses. No ill effects have occurred through this practice.

COMPLICATIONS

Pulse and blood pressure

Using former techniques of administration of steroids associated with the transfusion of large volumes of fluid, it was usual for anaesthesia to be accompanied by varying degrees of tachycardia. With the present technique it has been noted that there is usually no increase in pulse rate except when anaesthesia has been supplemented with gallamine. The conclusion that may be drawn from this is that the tachycardia was due rather to the large volume of fluid suddenly introduced into the circulation than to the steroid.

There is a definite tendency for moderate degrees of hypotension to occur and in some cases there has been hypotension to below 100 mm. of mercury. In all cases the skin remains pink and warm, capillary refill time is good and the veins are not collapsed. In all cases where the blood pressure has fallen it has returned to 100 mm. of mercury or above by the end of operation.

Although vasopressors will rapidly counteract any hypotension I have never had occasion to use them. Apart from ensuring adequate oxygenation and elimination of carbon dioxide, together with blood transfusion to maintain circulating blood volume should haemorrhage occur, no active steps are taken to counteract hypotension.

Hypotension is more likely to occur in the hypertensive patient.

In most cases there is a marked absence of capillary oozing and the quiet operative field obtained is something to be desired.

Respiratory depression

As described earlier, tidal volume is reduced soon after induction but this is of short duration and where necessary respiration is easily assisted or controlled during this period.

It has been noted that the period of apnoea or depression of respiration is usually prolonged after relaxant drugs have been given, and this is almost certainly due to the potentiation of these drugs by the Presuren.

Whenever relaxant drugs have been given, atropine and neostigmine have been administered at the end of operation.

When smaller doses of Presuren have been administered, e.g., 0.5G as cover to a patient having a caudal block—this respiratory depression has not occurred.

Thrombosis and phlebitis

During the early stages of this series five cases of slight tenderness over the vein at the site of injection occurred and there were four cases of severe thromboses. In none of these cases was procain administered following the Presuren. All cases responded rapidly to the application of dry heat and all were undoubtedly due to errors in technique. In one case where some Presuren was inadvertently administered extravenously, the site was infiltrated with procain and dry heat applied. Apart from slight redness of the skin no complications ensued.

I am sure that if the following rules are strictly applied no thromboses will occur—

1. A large vein must be used.

2. The Presuren must be administered warm and injected rapidly through a large bore needle.

3. Venous stasis must be avoided.

4. Administration of Presuren should be followed by the slow injection of 1 per cent. procain or procain added to the Presuren solution.

5. If possible not more than two injections of Presuren should be given into the same vein.

6. Any adjuncts that might be given should be injected into a separate vein.

ILLUSTRATIVE CASES

Case 1

Female aged 34 years. An asthmatic suffering from acute appendicitis. Had had attacks of asthma during the two days prior to operation. Premedication with pethidine 100 mgms. and atropine 0.4 mgm. Induction with Presuren 1 G., followed by routine nitrous oxide oxygen. Gallamine 80 mgms. given immediately peritoneum opened. Anaesthesia uneventful.

Case 2

Female aged 81 years. Frail old lady suffering from obstructive jaundice. Blood pressure 200/100 mm. of mercury. Past history, nephrectomy fifteen years ago. Premedication with Omnopon 10 mgms. atropine 0.4 mgm. Induction with Presuren 1 G. followed by routine nitrous oxide-oxygen and intubation without relaxant. Given 30 mgms. gallamine as soon as peritoneum opened. At laparotomy found to have carcinoma of ampulla of Vater. Cholecystectomy, choledoco-jejunostomy and entero-anastomosis performed. Awake at end of operation. Duration anaesthesia two hours. Anaesthesia and convalescence uneventful.

Case 3

Female aged 21 years suffering from congenital heart disease probably Fallot's tetralogy. Grossly cyanosed, clubbing fingers and toes, grossly abnormal E.C.G. For craniotomy because of intracerebral haemorrhage. Induction with Presuren 1 G. followed by nitrous oxide-oxygen 4 litres each. Intubated without relaxant. Craniotomy performed and intracerebral abscess drained. Duration of anaesthesia two hours. No further Presuren given and no relaxant. Original flow rates maintained throughout operation. Monitoring of the E.C.G. throughout operation showed no change. Anaesthesia and convalescence uneventful.

Case 4

Female aged 60 years suffering from intestinal obstruction. Blood pressure 180/100 mm. of mercury. No premedication. Emergency induction with Presuren 1 G. followed by routine nitrous oxide-oxygen and intubation without relaxant. D-tubocurarine (15 mgms.) given after peritoneum opened. Internal hernia reduced at operation. Anaesthesia and convalescence uneventful.

Case 5

Female aged 41 years suffering from carcinoma of breast. Blood pressure 140/90 mm. of mercury. Premedication Omnopon 20 mgms. atropine 0.6 mgm. Induction with Presuren 1 G. followed by nitrous oxide-oxygen. Intubation without relaxant. Operation lasted two and one half hours during which a further 0.5 G. Presuren administered. Blood pressure fell to 90/60 mm. of mercury thirty minutes after induction. Anaesthesia was otherwise uneventful and the blood pressure had risen to 120/80 mm. of mercury at end of operation.

ANALYSIS OF CASES

In the present series of cases, Presuren has been administered to 289 cases. Of these 45 were undergoing ophthalmic operations under Presuren without supplementary nitrous oxide-oxygen. In 19 of these anaesthesia with Presuren alone was not satisfactory and these

were supplemented with small doses of thiopentone. I feel that if a supplementary dose of Presuren had been given the thiopentone would not have been required.

Of the remaining 244 cases Presuren together with nitrous oxide and other supplements was administered to 166 and Presuren —nitrous oxide—ogygen without further supplements to 78 cases.

Ninety-eight consecutive cases were intubated without relaxant.

Presuren was administered to 19 emergency cases, 8 of which were suffering from intestinal obstruction. In none of these was the patient postured prior to intubation and in none did any vomiting occur.

Ages of patients has varied from 14 years to 93 years of age and the dosage has varied from .05G to 3 G. It has been noted that, as with other anaesthetic drugs the young and fit patient requires relatively larger doses. than older, sick and cachectic patients.

In addition Presuren in a dose of 0.5G has been administered to 22 patients undergoing various procedures under caudal or spinal analgesia. None of these received supplementation except the Wertheim hysterectomy to which nitrous oxide-ogygen was also administered. These cases are not included in the above figures.

	Caudal	*Spinal*
Vaginal hysterectomy	6	
Wertheim's hysterectomy		1
R.V.O. (Fothergill)	5	
Haemorrhoidectomy	7	
Prostatectomy		3
	18	4

CONCLUSIONS

Presuren may be administered in concentrated (5 per cent.) solutions provided that it is injected in warm solution and followed by the injection of procain.

TYPE OF CASE

	A	B
Head and neck operations	88	35
Radical mastectomy	12	10
Simple mastectomy	2	2
Thoracotomy	3	—
Oesophagectomy	2	—
Total gastrectomy (transthoracic)	5	—
Partial gastrectomy	5	—
Cholecystectomy	9	—
Appendicectomy	3	—
Colectomy	3	—
Hiatus hernia (transthoracic)	3	—
Herniorrhaphy	7	4
Incisional hernia	2	—
Subphrenic abscess	1	—
Bilateral adrenalectomy and oophorectomy	8	—
Unilateral adrenalectomy	2	—
Laparotomy	7	2
Abdomino-perineal excision rectum	3	—
Nephrectomy	2	1
Prostatectomy	2	—
Burst abdomen	2	—
Skin grafts	2	2
Strangulated hernia	2	—
Gynaecological operations	23	9
Caesarian section	5	1
Orthopaedic operations	34	9
Varicose veins	12	3
TOTALS	244	78

"A"—Total number of cases, excluding ophthalmic operations.

"B"—Cases receiving Presuren and nitrous oxide-oxygen only.

EMERGENCIES

Appendicectomy	3
Craniotomy	3
Caesarian section	4
Laparotomy (intestinal obstruction)	4
Ruptured abdomen	2
Strangulated hernia	3
	19

Intubation may be performed under Presuren, nitrous-oxide—ogygen anaesthesia without relaxant drugs and adequate anaesthesia may be maintained without supplementary anaesthetic or analgesic agents or relaxants.

The marked synergism between Presuren and nitrous oxide allows to be used to the full and analgesic and anaesthetic properties of that agent and to achieve adequate anaesthesia without anoxia. In many sick and bad risk patients it is possible to produce ideal operating conditions and to use a non-toxic combination of agents without the risk of anoxic episodes.

The apparent protection from shock is shown by the excellent post-operative condition of the patient and this is advantageous in the fit patient undergoing a major surgical procedure as well as in the aged and bad risk case.

The rapid and maintained suppression of laryngeal and pharyngeal reflexes even under light narcosis removes the necessity of administering relaxant drugs merely to maintain an endotracheal tube in position and this makes Presuren the anaesthetic of choice in surgery of the head and neck and whenever operating conditions necessitate intubation of the trachea.

The absence of bronchospasm makes it an ideal agent for the asthmatic, chronic bronchitic and those suffering from emphysema.

Presuren has been administered to 19 emergency cases (including 8 cases suffering from intestinal obstruction) and in none of these has there been any vomiting during induction of anaesthesia. Although this is a small number from which to draw conclusions its use may remove one of the great hazards of such cases.

Again, although it has been administered to only a few obstetric cases, satisfactory operating conditions were provided in all and there was no apparent effect on the foetus. If one subscribes to the view that all obstetric operative emergencies should be intubated, Presuren is likely to prove the drug of choice.

Presuren has proved ideal as a "cover" for those patients receiving caudal blocks or spinal or epidural analgesia. Previously one has been faced by the nervous patient having to be given a block while awake or alternatively having to first be given a sleep dose of thiopentone with the consequent difficulty of maintaining an adequate airway usually without expert assistance and with the ever present risk of laryngeal spasm. With Presuren the patient is given 0.5G immediately he arrives in the theatre and postured while awake. By the time the anaesthetist is ready to begin administration of the local analgesia the patient is asleep.

ACKNOWLEDGMENTS

The co-operation of Drs. Hudson and Saunders, my surgical colleagues and the theatre staffs of the Royal Perth Hospital and St. John of God Hospital, Subiaco, is gratefully acknowledged.

The Presuren used in this trial was generously supplied by Schering, A. G., and I should like to express my thanks to Mr. Earl Brown, of Schering, A. G. (Sydney) for his help and co-operation.

REFERENCE

STEDTFELD, G. (1957), *Anaesthetist*, vol. 6, page 113.

TRAUMATIC INTRAPERITONEAL RUPTURE OF THE URINARY BLADDER

By B. HARTLEY

Launceston General Hospital, Launceston

THE following case of intraperitoneal rupture of the urinary bladder is reported because it illustrates most of the textbook features of the condition and some of the difficulties in its diagnosis.

Case Report

A 33 years-old labourer was admitted at 4.30 p.m. on 16 Oct. 1957. On the previous day he had indulged in a beer drinking session, lasting from 5.30 p.m. to 9.30 p.m., and later that night had become involved in a fight. He was unable to remember details of the incident, but knew that, at one stage, he had received either a blow or a kick in the abdomen. He reached his room and slept well that night. At 11.30 a.m. next day he awoke with abdominal pain. He was not sure of its initial site, but it gradually became more severe, was of a constant nature, was aggravated by coughing, and did not radiate. There was no pain in his shoulders. A few ounces of heavily blood-stained urine were passed on two occasions that morning.

There were no gastro-intestinal symptoms, except that he had vomited once en route to the hospital.

There were no relevant features in the family or previous history.

On examination, the man was found to be sweating and in severe pain. He was breathing rapidly and shortly in an effort to minimize his pain. His face was flushed and rather plethoric. He had a "black eye" and a subconjunctival haemorrhage on the left side. There was a laceration over the left side of his forehead. No bruises or other signs of contusion were seen in the abdomen or over the perineum. The abdomen was rigid and tender all over. One observer thought that the maximum tenderness was in the suprapubic area. Bowel sounds were absent and shifting dullness could be demonstrated; this latter with some difficulty. Rectal examination revealed no abnormality. The respiratory, cardio-vascular and central nervous systems all appeared normal. Temperature 99.2° F. Pulse 84/m. Respirations 26/m. Blood pressure 140/80 mm. of Mercury. Haemoglobin (by Sahli method) was 100 per cent.

X-ray films of the chest, lumbo-sacral spine and pelvis were all normal. Supine and erect films of the abdomen showed no abnormality; no free gas was seen within the peritoneal cavity. Intravenous excretory urography was undertaken. The dye was excreted well on both sides. The calyceal systems and pelves of the kidneys and the ureters all appeared normal. The shadow of the bladder was also interpreted as being normal (Fig. I).

The patient had been unable to void since admission and it was decided to postpone catheterization until he was taken to the operating theatre.

There, after the induction of anaesthesia, a soft urethral catheter was passed. A few drops of macroscopically clear urine were obtained, and this amount was increased by suprapubic manual compression. Later, the urine was found microscopically to contain many red blood cells.

Despite the normal cystogram and the apparently clear urine, the surgeon still thought a ruptured bladder the most likely diagnosis.

Operation

A right lower paramedian incision was made. When the peritoneum was opened it was found to contain a considerable quantity of fluid, which had the appearance of urine. The bladder itself was rather small and contracted. Further exploration revealed a transverse tear in its superior part, about 1½ inches long. The edges of the split were not bleeding, as they were sealed by a small quantity of blood clot. The rent was closed with interrupted catgut sutures through the whole thickness of the bladder wall, and a wide-bore suprapubic drainage tube was brought out through a stab wound in the anterior wall. As much as possible of the remaining urine was removed from the peritoneal cavity by gentle suction. The other organs of the peritoneal cavity were explored carefully, but no other abnormality was found. It was then closed, a corrugated rubber drain being brought out through the middle of the incision. The wound was closed in layers, interrupted sutures being used.

Post-operation

A Rehfus naso-gastric tube was passed and intermittent suction instituted. The intravenous infusion of fluid which had been started during the operation was continued. This and the suction were stopped after three days, when normal bowel sounds were heard. Procaine penicillin 500,000 units and streptomycin 0.5 Gm. twice daily were given for five days. The peritoneal drainage tube was removed after three days, and the suprapubic after five. When the latter was removed a No. 18 Foley self-retaining urethral catheter was inserted. It was kept in situ for a

further ten days, and sulphadimidine tablets (0.5 gms. six-hourly) were given during this period. Both the suprapubic and main wounds healed cleanly. The patient was discharged after 15 days in hospital. Since then he has been quite well and has had no urinary symptoms.

FIG. I. Film of lower urinary tract 10 minutes after injection of 20 cc. of Urografin. The opacity near the right ischiac spine is due to a screen mark.

DISCUSSION

Traumatic rupture of the bladder is a comparatively rare peace-time injury, being less common than injury to the liver, spleen or kidney (Aird, 1957).

It may occur in two ways:—

(a) The bladder may be split from inside as a result of a sudden increase in intravesical pressure; or

(b) be perforated from outside by a fractured adjacent bone or by foreign body.

The first type results most commonly from blunt trauma to the anterior abdominal wall. This causes a sudden rise of intraperitoneal pressure, which is in turn transmitted to the bladder. If a tear results, it will be intraperitoneal only if the bladder is full and if the patient is a male or a child. In the female, the bladder, even when full, is more extrathan intraperitoneal, and therefore intraperitoneal rupture is extremely rare. Toole (1947) in a review of the literature could find only five cases. The trauma may be the result of a fall, a fight, or accident. Inebriation is often an accompaniment, for the bladder is well filled by the alcoholic diuresis and, should a blow be received, the lax tone of the muscles offers little protection. The tear generally occurs in the superior part of the bladder, just at the junction with the posterior wall; probably because this section is the least well supported.

Other rarer cases of rupture, due to rise in intravesical pressure, have been listed by Ross (1944):—

(1) during parturition:

(2) injury due to a lithotrite, excessive diathermy or a resectoscope:

(3) over-distension during cystoscopy:

(4) spontaneous rupture of the diseased bladder:

(5) spontaneous rupture of normal though distended bladder:

(6) secondary to osteomyelitis of the spine:

(7) secondary to urethral stricture:

(8) secondary to manipulation of fractured pelvis:

(9) following trivial falls, exertions or twists.

The second type of injury is usually caused by fractures of the pelvis. Here, again, the anatomical relations explain the route which the extravasated urine takes. Usually it tracks extraperitoneally.

Penetrating injuries, which are rare in peace-time, may cause either an intra- or extraperitoneal injury, or both, depending upon the site of entry and the track of the missile.

Clinical features

A history of the nature and site of the injury is frequently given, but in alcoholic patients this may be sketchy, inaccurate, and perhaps unobtainable. With children, also, the history may be very poor.

Inability to void following the injury is a common complaint. However, as illustrated in the reported case, is by no means an invariable feature. Giebert and Dodson (1951) found that 13 per cent. of cases with a ruptured bladder and 40 per cent. of cases with ruptured urethra were able to pass urine. If urine is passed, it is almost always blood-stained.

Low or generalized abdominal pain is present and accompanied by rigidity. Free fluid within the peritoneal cavity may be demonstrated. If twelve hours have passed since injury, the signs of peritonitis will be found and are often associated with paralytic ileus. The shock often found is a result of peritoneal soiling by urine alone or as a result of peritoneal soiling plus blood loss.

The degree of blood loss will depend largely upon the anatomical site of the tear. If, as in the present case, it is in the lax part of the bladder, contraction of muscle fibres takes place fairly rapidly and blood loss is slight. Should the tear extend into the side wall of the bladder, it may involve larger and more fixed blood vessels and the blood loss will then be considerable.

The reasons for the dramatic and drastic effects of urine within the peritoneal cavity are not clear. Peritonitis will obviously result from previously infected urine, but it is not usually stated why sterile urine causes such serious changes. Small quantities, injected at intervals, do not cause peritonitis. Continuous drainage of urine into the peritoneum, in contrast, rapidly leads to death. Ross (1949) reports a case of a native who died four days after receiving the injury; at necropsy there were no signs of excessive blood loss. It seems unlikely that simple absorption with uraemia is the cause, for patients with anuria usually survive for longer periods. Irritation will cause loss of extra cellular fluid into the peritoneal cavity, but excessive fluid in the peritoneum has not been a feature of reported post-mortems.

Diagnosis

The diagnosis of injury to the genito-urinary tract is usually first suggested by a history of inability to void or of haematuria following a blow. The presence of intraperitoneal free fluid within the rigid abdomen of a shocked patient with no demonstrable sites of blood loss will point to this diagnosis, even in the absence of a history. In all cases it must be kept in mind that other intraperitoneal lesions may be present, complicating and confusing the picture.

The following routine is suggested as a plan for further investigation where rupture of the bladder or urethra is suspected:—

1. X-ray film of the chest:

This may demonstrate an associated injury of the thoracic cage, of the diaphragm, or of the lungs themselves.

2. Plain X-rays of the abdomen; erect and supine.

These films are inspected for such features as fractures of the 12th rib, fractures of the transverse processes or bodies of the lumbar vertebrae, the absence of the normal psoas and/or renal shadows as a result of haemorrhage from the kidney and meteorism of the bowel over the site of a ruptured kidney. They will also demonstrate free gas in the peritoneal cavity, should it be present, and will warn of an associated paralytic ileus. The bones of the pelvis are especially scrutinized for fractures.

3. Intravenous excretory urography.

Before any operation is undertaken on the urinary tract, all efforts should be made to show whether the patient has two, one, or no functioning kidneys. This is the simplest way to find out and is an essential step in the procedure. Because a shocked patient has a lowered renal blood-flow, the dye may not be excreted effectively. Shock must, therefore, be treated and the blood pressure raised to normal before the injection is given. The site of a lesion in the genito-urinary tract may be located exactly. Normal films can, however, be deceptive, as in our case, and should be accepted with reserve. The reasons for apparently normal films in the presence of a ruptured bladder are:—

(a) the urinary secretory rate of 1-2 cc./min. may not produce enough urine to distend the bladder and cause a leak:

(b) the leak may be temporarily plugged by a loop of bowel, and

(c) the large bladder shadow may obscure a small lateral extravasation.

For this last reason oblique, as well as antero-posterior views, should always be taken.

If these urograms show no abnormality, the next procedure is carried out.

4. Retrograde cystography (Prather, 1954).

A soft rubber urethral catheter is passed under sterile conditions and 150 cc. of 15 per cent. diodone (Perabrodil) solution are injected. Antero-posterior and oblique views are taken. It is important to take another film of the bladder after an attempt has been made to withdraw the solution. A small extravasation, previously obscured by the larger shadow, may be seen.

5. Urethrogram.

If the sterile catheter cannot be passed and there is a history of haematuria or bleeding from the bladder, the possibility of a ruptured urethra must be considered. To demonstrate its site 20 cc. of 60 per cent. Urografin (sodium and methylglucamine salts of 3.5 - diacetylamino- 2,4,6 triiodbenzoic acid) are injected from the urethral meatus. Again, antero-posterior and oblique films are taken.

Treatment

The principles of treatment are:—

(1) To combat the associated shock.

(2) To make an early and accurate diagnosis.

(3) To divert the flow of urine from the peritoneal cavity.

(4) To drain urine from the fascial spaces into which it may have extravasated.

(5) To prevent the onset of, and treat, any infection by means of antibiotics.

(6) To prevent and treat the paralytic ileus often also present.

Operative considerations

A lower median incision gives the best exposure. The bladder is carefully inspected to determine the site and size of the tear. Before repair is started the positions of the ureter orifices are found; if necessary, by the use of an intravenous injection of indigo-carmine. Care can then be taken to see that they are not caught up in the reparative sutures. The rent is closed, using interrupted sutures through the whole thickness of the bladder wall. The peritoneal cavity is cleared of urine by gentle suction and a careful examination of the other peritoneal structures is made. The cavity may or may not be drained.

A suprapubic drain is inserted through the anterior wall of the bladder in all cases (Mogg, 1947). An in-dwelling catheter should not be used, as drainage by this means is uncertain. The small eye easily becomes blocked by mucous or blood clot, and the catheter then becomes a plug instead of a drain. Moreover, it cannot be left *in situ* long enough for the bladder to heal and for infection to be controlled.

The extraperitoneal tissues of the bladder are inspected and the space of Retzius is drained.

TABLE 1

MORTALITY RATES IN BLADDER INJURY

(Bailey, 1940)

Interval between injury and operation	*Mortality Rate*
12 hrs.	11 per cent.
24 hrs.	55 per cent.
Untreated	100 per cent.

Prognosis

Hippocrates' aphorism states, "A severe wound of the bladder . . . is deadly" (Adams, 1939). Ross's (1949) case suggests that, in the untreated patient, it is still true. Hamilton Bailey (1940) stated that the mortality rate is related to the interval between the receipt of the injury and the time of operation (Table 1). More recent writings suggest that nowadays all treated patients do well. Michels (1946), reporting on war injuries, showed that in 21 cases of uncomplicated bladder injury no death occurred. Ross (1944) notes that all cases subsequently develop some degree of cystitis.

SUMMARY

The prognosis of intraperitoneal rupture of the bladder is known to be improved by early operation. Early diagnosis is therefore essential. A clinical triad of injury, inability to void, and lower abdominal pain will always suggest it, but is not always found. Radiographic methods are a great help, both in the localization of the lesion and in the demonstration of other accompanying injuries. These methods also have their limitations; however, the use of a carefully planned routine will give a great deal of valuable information. Treatment is both local and general. Supra-pubic drainage of the bladder should be used whenever possible.

A typical case has been presented.

ACKNOWLEDGEMENTS

I wish to thank Mr. R. P. Booth, under whom the patient was first admitted; Mr. D. I. Roberts, to whom the patient was later transferred; the Board of Management of the Launceston General Hospital, for permission to publish the case history: and Dr. C. Craig, who kindly read my manuscript and made helpful suggestions.

REFERENCES

ADAMS, F. (1939), "The Genuine Works of Hippocrates". Baltimore, Williams & Wilkins Co.

AIRD, I. (1957), "A Companion in Surgical Studies". 2nd edit. Edinburgh. E. & S. Livingstone Ltd.

BAILEY, H. (1940), "Emergency Surgery". 4th edit. Bristol. J. Wright & Sons Ltd.

GIEBERT, D. R., and DODSON, A. I. (1951), *West Va. med J.*, vol. 47, page 359.

MICHELS, I. M. (1946), *Ann. Surg.*, vol. 123, page 999.

MOGG, R. A. (1947), *Proc. roy. Soc. Med.*, vol. 40, page 795.

PRATHER, G. C. (1954), *J. Am. Med. Ass.*, vol. 154, page 205.

ROSS, J. C. (1944), *Brit. J. Surg.*, vol. 32, page 44.

ROSS, W. F. (1949), *Brit. med. J.*, vol. 2, page 368.

TOOLE, C. F. (1947), *J. Urol. (Baltimore)*, vol. 58, page 431.

Books Reviewed

MEDICINE AND THE NAVY, 1200-1900.

Volume II. 1649-1714.

By J. J. KEEVIL, D.S.O., M.D. Edinburgh: E. & S. Livingstone Ltd., 1958. 9" x 6¼", xii plus 332 pp., 18 plates. Price: 40s. (stg.).

The first volume of this work covering the years between 1200 and 1649 was reviewed in the February, 1958, issue of the *Journal* and its excellence noted. The second volume covers a much shorter period but into that sixty-five years is crammed an enormous amount of naval history; indeed it is the period which marked the birth of the modern Royal Navy, a period made familiar to us by Samuel Pepys. Unfortunately Surgeon Commander Keevil did not live to see the second volume in print or even in proof but he has written a magnificent amount of the trials and tribulations of the Naval Medical Service from 1649 to 1714. He gives a most vivid picture of the care of the sick and wounded during the three Dutch wars and the Spanish war, of the apathy of the Naval Board to medical matters and of the attempts of the sea-surgeons to cope with their difficulties. Sick and wounded had to be evacuated to civil hospitals at the coastal ports and even to London to St. Thomas's and St. Bartholomew's Hospitals. It was a period of great expansion in the Royal Navy but it is quite obvious that the medical services did not expand as quickly as other sections of the Navy. It was to be many years before naval hospitals were established. To man the newly built ships and to replace casualties untrained men were pressed into the service; those that were verminous or sick quickly spread typhus and other diseases to the rest of the crew.

Because the Navy had established foreign bases, notably in the West Indies, hospital ships were introduced in 1654. The ravages of scurvy together with the high mortality and morbidity from illness and wounds is vividly told, as are the hardships of service life and the individual endeavours of the surgeons to improve conditions. It is interesting to note that, when the plague hit London in 1665, quarantine was practised by the Navy. The bad pay and, perhaps what was more important, the uncertainty of payment, together with the bad conditions did not produce many volunteers for the medical service; medical officers often had to be pressed into service like the men.

This volume covers a period which is far better documented and so we meet many personalities. Among these is James Yonge who joined the Naval Medical Service as an apprentice to a naval surgeon when he was but eleven years old and who kept a most interesting and informative diary during his long service.

Daniel Whistler, John Knight, James Pearse, Richard Lower, William Cockburn and James Christie all did much for the Naval Medical Service in various capacities and their story is well told. It was not until the close of the seventeenth century that long needed reforms were introduced into many branches of the service, but it was to be a long time before the voices of the surgeons were heard and heeded by those in authority.

This volume is a very worthy successor to the first; both will, for a very long time, be the authority for the history of the Naval Medical Service up to the start of the eighteenth century. It is a matter for great regret that Surgeon Commander Keevil was not spared to complete his work.

FRACTURES AND OTHER INJURIES:

Edited by EDWIN F. CAVE, M.D. Chicago: The Year Book Publishers Inc., 1958. 10" x 7", xvii plus 863 pp., 612 illustrations. Price: $28.00.

This is a comprehensive and impressive account, of reasonable length, of fractures and other injuries such as those to the skin (burns), tendons, nerves, blood vessels, the brain and spinal column and cord, the abdomen and chest and so on. Furthermore, there are short and important chapters on general principles such as the metabolic response to trauma which is a clear and straightforward account of the reaction of the metabolisms of nitrogen, the electrolytes, the carbohydrates and the many other specific substances that are involved. But the book is largely confined to fractures and therein lies the main message. It is written by 39 authors, many of whom have taught in the annual post-graduate course given by members of the Fracture Clinic of Massachusetts General Hospital under the auspices of the Faculty of the Harvard Medical School. The Fracture Clinic at the Massachusetts General Hospital was established in 1917 by Charles L. Scudder and was the first such clinic in the United States. Although there are so many authors the editorial board has exercised skill, industry and artistry in compressing the material to essential matters and at the same time preserving a uniformity and orderliness throughout the book that it has the balance of the single author, if not more so. For example, in each chapter a systematic order is followed with descriptions of the anatomy, clinical examination, X-ray examination which is illustrated by clever line drawings of the technique whenever there are special radiographic views such as demonstrating a fracture of the posterior acetabular rim, methods of closed reduction (again with clever line drawings) and so on. The indications, contra-indications and again the justifiable or doubtful indications for open reduction are discussed with an objectivity that one might expect from experienced instructors to the post-graduate students and who are writing for the general guidance and direction of others. A valuable and unusual feature is the description of all recommended operations which are illustrated by numerous and detailed series of drawings, many with original features. The section on the hip is masterly as might be expected. In this, is the type of conservative advice that prevails, as a rule, throughout the book. Nailing of the impacted fractured femoral neck is not advised. It may cause disimpaction. "Rarely, however, does the femoral neck fracture that is truly impacted in valgus fall apart." The part on forearm fractures, with the editor as co-author, is excellent. The influence of post-graduate

instruction in the birth of this book is shown in the two pages of illustrations in the section on Colles' fracture to show the trap of the co-existence of another fracture such as the head of the radius or humerus in the same limb. Removal of the carpal navicular for non-union is condemned out of hand as indeed it was by Böhler twenty-five years ago and who recently repeated that the operation was "crippling." Internal fixation for open fractures is not advised. "A safe and reasonable procedure is: first allow the wound to heal, and then apply internal fixation if necessary." These are some few examples of the prudence and wisdom that are presented to the reader. Although the book is written by eminent specialists who advise and describe their own choice of practice, it does not appear to be written so much for the specialist — although he will learn a great deal and find the possession of the book a valuable one — but for those surgeons seeking guidance and direction, not only as to a selection of procedure but also the details of carrying that out. This may have a special message for the surgeon, especially in this large land where the population is spread thinly, although widely, and who, of necessity, has to be resourceful.

AN INTRODUCTION TO EXPERIMENTAL SURGICAL STUDIES.

By W. J. DEMPSTER, F.R.C.S. Oxford: Blackwell Scientific Publications Ltd., 1957. 8¾" x 5½", 463 pp., 71 illustrations. Price: 50s. (stg.).

If John Hunter were happily still surviving, he would observe with some satisfaction that the habit of tackling the problems of surgical practice in the laboratory is a growing one.

The author of this monograph is a fully trained surgeon, who early in his career embarked on such an exercise and who has since served a rigorous apprenticeship in this field.

It is, however, fully apparent from a perusal of this volume that a partial retreat to the laboratory has in no way lessened his ability to keep himself completely abreast with every new development in the practice of surgery at the bedside.

In his preface he states that it is his aim "to provide a wide range of references and a critical commentary which together should form a sort of springboard from which the young experimentalist can take off into his own researches." In this he has succeeded quite admirably. A random search for a line of enquiry on a variety of surgical problems gave a very satisfactory yield in terms of source articles and equally helpful and stimulating guidance in the text; the bibliography in range and in variety is itself an index of the width of his research interest.

It is true that a young research worker mainly interested in gastro-enterology might legitimately complain that the coverage in this field is niggardly when compared with the attention given to tissue grafting and transplantation, which occupies rather more than a quarter of the entire text.

It is, however, inevitable that any monograph should represent in some degree the primary interests of the author and Mr. Dempster has made some notable contributions to the literature on these subjects. Moreover, if this is not excuse enough, it can still fairly be claimed that research in this direction is among the most exciting and seems likely in the fullness of time to be most fruitful.

It is a delight to review a book on experimental surgery for this is something quite new in British surgical writing. It deserves as a dividend, not only quick sales, but a worthwhile recruitment of young surgeons intent on following what the author calls . . . "the systematic investigation of a surgical problem by comparative anatomy and physiological means."

Is it too much to hope that success of this, his first authorship, may encourage Mr. Dempster to tackle a companion volume on technique in experimental surgery?

SURGERY OF THE CHEST.

By JULIAN JOHNSON, M.D., D.Sc.(Med.), and CHARLES K. KIRBY, M.D. Second Edition. U.S.A.: The Year Book Publishers Inc., 1958. 8½" x 6", 398 pp., 86 plates. Price: $9.75.

This is the second edition of this work, with major additions in the section of cardiovascular surgery. The preface states that the book is primarily an atlas of thoracic surgical operations and that the objective has been to present the step by step details of operative technique in as clear a manner as possible. This aim has been achieved and the illustrations are excellent.

Surgical techniques vary and no book of this nature could please all thoracic surgeons. It would seem that some of the differences in techniques described from those practised in Australia are due to considerable differences in chest anaesthesia and chest physiotherapy. To Australian readers it will seem odd that the statement that some patients do not tolerate controlled respiration well occurs more than once, with the implication that such patients stand some other (unspecified) anaesthetic technique better, and that one lung anaesthetics and bronchial blockers are not mentioned. Evidently they are not provided by the authors' anaesthetists. Presumably this is why so much stress is placed on positions of the patient on the operating table to reduce the risk of "spillover" of secretions. Here we rely on our anaesthetists to protect our patients from this risk and we always use the lateral position when this gives the most convenient surgical approach. It would also appear that chest physiotherapy is little used by the authors. Postural drainage is mentioned but there is no reference to breathing and postural exercises. Perhaps this is why they sometimes find it necessary to divide three intercostal nerves above and below the incision to diminish post-operative pain.

In the illustrations and in the text the impression is repeatedly given that longish bronchial stumps are desirable. For instance it is recommended that in right upper lobectomy the three segmental bronchi should be divided and sutured separately. No British-trained surgeon could accept this. We believe that bronchial stumps should be sutured leaving no blind *cul de sac*. Also, segmental resection of tuberculous lesions has been practised here for the last eight years with good results, so that the statement that "the advisability of segmental resection for tuberculous lesions has not yet been definitely established except for small tuberculomas" is, to us, surprising. For permanent drainage of chronic empyemas and for cavernostomies the very valuable procedure of turning in a skin flap and suturing it to the parietal pleura is omitted and hydatid disease, common in this country, is not mentioned.

These and other less fundamental differences from Australian practice detract somewhat from the value of the sections on pulmonary surgery to Australian surgeons, but the sections on oesophageal and cardiac surgery are much more acceptable and the book will be of great help to surgeons embarking on their apprenticeship in the specialty of thoracic surgery.

ENDOCRINE ASPECTS OF BREAST CANCER: (Proceedings of Conference, Glasgow, 8th to 10th July, 1957.

ALASTAIR R. CURRIE, B.Sc., M.B., F.R.C.P.Ed., Editor. Edinburgh and London: E. & S. Livingstone Ltd., 1958. 8¼" x 5½", xvi plus 344 pp., various tables and 24 illustrations. Price: 37s. 6d. (stg.).

In every field of human endeavour there is a changing emphasis, determined largely by the development of new techniques. The focus of interest in cancer of the breast has recently turned towards those factors within the body of the patient which influence the growth of the tumour. A vast amount of research on the endocrine aspects of breast cancer taking place in many laboratories in many countries was reviewed at a conference at the University of Glasgow in July, 1957. The 45 papers presented, together with notes on the discussions which followed, are published as a book.

The papers are grouped into four sections, with a summary at the end of each section, and also at the end of some sub-sections. Workers in the different fields present their own experiences and review their results in relation to those of others. In the clinical section the opening papers on the results of adrenalectomy in cancer of the breast are presented by Sir Stanford Cade and by Hellstrom and Franksson in Stockholm. Experiences with hypophysectomy and other methods of destroying the pituitary (implantation of yttrium – 90, radio-active gold or ^{32}P, section of the pituitary stalk) are related in a series of papers. The results are compared with those following adrenalectomy, and the section concludes with the consideration of the physiological and metabolic effects of the removal of these ductless glands.

The section on pathology deals with some histological and chemical studies on the pituitary, adrenal and mammary glands and this inter-relationship. Fifteen papers present a large amount of information about the pattern of hormone production in breast cancer and the effects of removal or obstruction of the various endocrine glands. One sub-section considers the hormones of the anterior pituitary in relation to the breast, another the excretion of oestrogens in the urine after adrenalectomy, oophorectomy and hypophysectomy; methods of analysis of urinary oestrogens are compared. A third sub-section deals with urinary 17-oxosteroids and presents opposing evidence and views as to the prognostic value of this estimation in cancer of the breast.

In a final section of experimental pathology nine papers review the evidence of the relation of pituitary hormones to the growth of the breast and the relation of mammary tumours in mice, to a variety of hormones. An analogy is drawn between experimental tumours in mice, which are dependent on progesterone, androgen and oestrogen levels, and some tumours of the human breast which are found to be influenced by the hormonal state of the patient.

This review does no more than indicate the contents of the book.

A great deal of information is presented, but the significance of much of this is not yet determined. It is therefore considered unwise to select fragments for special comment. Surgeons and endocrinologists engaged in treating cancer of the breast should read these papers in their context and in relation to the discussions and summaries at the end of each section. All who are interested in extending their knowledge of the development and control of cancer should study the report of this conference in detail.

CLEFT PALATE AND SPEECH.

By MURIEL E. MORLEY. Fourth Edition. Edinburgh and London: E. & S. Livingstone Ltd., 1958. 7½" x 5". xx plus 271 pp., 83 illustrations. Price: 27s. 6d. (stg.).

The fourth edition of this very popular work has brought the subject matter further up to date and added substantially to the breadth of treatment of the subject. In fact, as in so many publications of a similar type, what began as a simple monograph for Speech Therapists has now become a very workman-like précis of most of the surgery, orthodonture and speech therapy related to the management of children born with cleft lips and palates.

This book has always been extremely popular, not only amongst speech therapists but as a reference for resident medical officers and surgeons too. Although one cannot avoid the feeling that works of this nature lose something of their merit when their scope is widened to include material which is not within the first-hand knowledge and experience of the author, nevertheless, Miss Morley's surgical advisors have been so freely used that it is difficult to make this criticism in this particular case and one must continue to recommend it as a work of very high quality.

SURGERY FOR NURSES.

By JAMES MORONEY, M.B., Ch.B., F.R.C.S.(Eng.), L.R.C.P.(Lond.). Fifth Edition. Edinburgh and London: E. & S. Livingstone Ltd., 1958. 8½" x 5½", xii plus 712 pp., 600 illustrations. Price 30s. (stg.).

Admittedly, one does not expect a book written for nurses to be a first-class textbook of surgery. However, surely it should aim to give instruction in a superficial but well-balanced fashion. Certain sections of this book can only be described as misleading to ingenuous readers. Surely no nurse should be told that carcinoma of the thyroid is usually treated by irradiation, nor that the perineal wound is packed open after removal of the rectum.

Attempts have evidently been made to bring the book up to date with a section on surgery of the heart and a whole page on hypophysectomy for carcinoma of the breast. This space, and that devoted to a section on obstetrics, could have been used better to enlarge on the treatment of burns, which is woefully brief.

In a surgical book, it is a surprise to learn that "auscultation is particularly valuable to the nurse in the diagnosis and control of auricular fibrillation."

Despite these criticisms ,the book remains a useful handbook for nurses. It is refreshing to see a good illustration of the correct sites for intramuscular injections.

Royal Australasian College of Surgeons

Proceedings

General Scientific Meeting, 1959

All Fellows of the College and Fellows and Members of the Faculty of Anaesthetists have been advised that the General Scientific Meeting for 1959 will be held in Sydney from the 18th to 21st August, 1959, and not in Brisbane as previously announced. The Inaugural Meeting will be held in the Great Hall, University of Sydney, on the evening of Tuesday, 18th August, 1959.

The theme of the meeting will be "Cancer." K. W. Starr, of 149 Macquarie Street, Sydney, has been appointed Convenor of the General Scientific Meeting Sub-Committee. Convenors of the various Advisory Sub-Committees in special branches of surgery are asked to communicate with him concerning suggestions for the programme of their particular sections. A preliminary programme, together with full details concerning the meeting, will be issued at an early date.

Primary Fellowship Examination, Singapore

The College will again conduct the Primary Examination in Singapore in March-April, 1959. Wide publicity has been given to the examination, which on this occasion, is not being conducted under the auspices of the Colombo Plan but by direct arrangement between the Government of Singapore and the College. The Government of Singapore has expressed great satisfaction at the action of the College in continuing this work.

International Federation of Surgical Colleges

In May, 1958, a meeting was held in Stockholm at which the International Federation of Surgical Colleges was founded. The Royal Australasan College of Surgeons is one of the Founder Members of the International Federation, and is a member of the first Executive Committee. I. B. Jose represented the College at the meeting.

Development Fund

At the last Council meeting it was decided that the corpus of the development fund shall be used firstly for building purposes and that the immediate need of the College is a modern and adequate lecture hall. It is however not intended to undertake such work until the fund reaches £50,000. In the meantime the income from the funds to be used for post-graduate teaching purposes, including such grants-in-aid as may be made to candidates who apply for and are considered worthy of this help.

It is the earnest hope of the Council that with proper growth of this fund these educational activities will become permanent and assured. The fund needs considerable support from the Fellows and from benefactors outside the College if it is to achieve the objects of the Council.

A list of donations to date is included with this report.

Courses of Instruction

Final Examinations to be held in May and October, 1959.

The N.S.W. State Committee, in conjunction with the Post-Graduate Committee, has arranged for a course in post-graduate surgery to commence on 2nd March for two months in preparation for the May examination. This course will occupy half of every day. Particulars may be obtained from the Honorary Secretary of the State Committee.

The Victorian State Committee is arranging a course in post-graduate surgery to be held in Melbourne from 3rd August to 9th October in preparation for the October examination. This course will be full-time; arrangements for work in the mornings will be made with the clinical schools, and the afternoons will be devoted to formal instruction and clinical sessions.

Particulars are obtainable from the Secretary of the College.

Courses for the Primary

An effort is being made to arrange post-graduate courses of instruction in anatomy, physiology and pathology in preparation for the Primary Examinations.

It is hoped that such a course will be held in Melbourne in preparation for the March examination, and in Sydney in preparation for the September examination.

Particulars may be obtained from the Secretary.

Alterations at the College

The basement of the College building has been converted into a permanent Examination Hall and in it are being arranged the unique museum collection of the Faculty of Anaesthetists, as well as our historical surgical instruments.

COLLEGE DEVELOPMENT FUND

The Council wishes to acknowledge the receipt of the following donations:—

AUSTRALIA

Anonymous	£21	0	0
Anonymous	5	0	0
J. P. Ainslie	50	0	0
Esmé V. Anderson	50	0	0
J. R. Barbour	100	0	0
Dr. J. E. Barker	10	10	0
E. V. Barling	20	0	0
H. C. Barry	100	0	0
J. D. Begg	10	0	0
George Bell	100	0	0
Dr. J. M. Bell	5	5	0
R. V. Blaubaum	100	0	0
J. S. Bothroyd	20	0	0
P. Braithwaite	50	0	0
C. J. Officer Brown	100	0	0
Edgar Brown	21	0	0
J. Grayton Brown	105	0	0
T. V. Stubbs Brown	105	10	0
D. D. Browne	30	0	0
British Tobacco Coy. (Aust.) Ltd. (per K. W. Starr)	100	0	0
L. Buchanan	5	5	0
Dr. Mary T. Burnell	20	0	0
K. B. Burnside	50	0	0
Dr. K. J. Byers	15	0	0
N. Campbell (per J. Grayton Brown)	26	5	0
E. T. Cato	2,020	0	0
Dr. R. Clark	10	0	0
J. H. Cloke	10	10	0
A. S. de B. Cocks	10	10	0
C. L. Coghlan	20	0	0
F. J. O. Colahan	10	0	0
Dr. W. H. J. Cole	5	5	0
J. B. Colquhoun	5	5	0
F. W. Connaughton	25	0	0
V. M. Coppleson	10	10	0
W. D. Counsell	20	0	0
R. A. Craven	20	0	0
Dr. H. J. Daly	10	0	0
Dr. G. M. Davidson	10	0	0
F. Ch. de Crespigny	10	0	0
Sir Hugh Devine	100	0	0
D. L. Dey	20	0	0
Sir Owen Dixon	105	0	0
C. D. Donald	95	5	0
H. D. Drury	20	0	0
E. E. Dunlop	100	0	0
Estate of late Sir Thomas Dunhill	500	0	0
H. G. Earnshaw	20	0	0
H. H. Eddey	100	0	0
Sir Benjamin Edye	100	0	0
F. F. Ellis	25	0	0
K. J. Fagan	20	0	0
Dr. K. Fairley (per C. J. Officer Brown)	12	12	0
A. W. Farmer	10	0	0
F. R. Fay	5	0	0
I. A. Ferguson	10	10	0
D. I. Fitzpatrick	5	0	0
S. C. Fitzpatrick	20	0	0
W. B. Fleming	20	0	0

Sir Kenneth Fraser	10	10	0
C. W. Gale	4	4	0
General Motors Holdens Ltd.	100	0	0
P. C. R. Goode	5	5	0
E. H. Goulston	20	0	0
E. J. Green	20	0	0
Dr. R. Greenlees (per C. J. Officer Brown)	52	10	0
P. H. Greenwell	10	0	0
W. R. D. Griffiths	50	0	0
G. S. Gunter	40	0	0
R. D. McK. Hall	10	10	0
B. R. Hallows	10	10	0
N. T. Hamilton	100	0	0
T. Hamilton	5	5	0
R. J. Hardstaff	10	10	0
H. H. Harrison	105	0	0
N. M. Harry	5	0	0
G. C. Hawker	25	0	0
W. I. Hayes	10	10	0
E. A. E. Hedberg	20	0	0
I. C. Heinz	10	10	0
A. F. Hobbs	50	0	0
J. Hoets	100	0	0
R. S. Hooper	10	0	0
Dr. G. Houseman	100	0	0
R. N. Howard	100	0	0
C. P. Hudson	10	0	0
Late Sir Victor Hurley	50	0	0
G. Hutchinson	10	0	0
H. M. Jay P. G. Jay	30	0	0
A. S. Johnson	10	10	0
Johnson & Johnson (per K. W. Starr)	525	0	0
I. B. Jose	141	18	0
P. J. Kenny	20	0	0
B. T. Keon-Cohen	20	0	0
R. H. Kernutt	10	0	0
Dr. P. Kinston (per J. Grayton Brown)	26	5	0
K. L. H. Kirkland	20	0	0
C. D. Langton	20	0	0
T. B. Law	10	0	0
R. S. Lawson	100	0	0
A. H. Lendon	20	0	0
Dr. F. Leventhal	10	0	0
Nancy Lewis	20	0	0
L. C. E. Lindon	50	0	0
Dr. V. Lines	5	0	0
L. S. Loewenthal	100	0	0
S. H. Lovell	26	5	0
R. F. Lowe	100	0	0
R. H. Macdonald	45	0	0
W. L. Macdonald	25	0	0
R. M. Macintosh	21	0	0
Dr. K. W. MacLeod	5	0	0
Dr. K. McCaul	7	0	0
H. K. McComb	10	0	0
Dr. J. F. McCulloch	25	0	0
A. C. McEachern	100	0	0
R. D. Marshall	10	0	0
Dr. S. V. Marshall	25	0	0
H. H. Martin	10	0	0
C. M. Maxwell	26	5	0
S. D. Meares	100	0	0
R. P. Melville	105	0	0
Douglas Miller	152	10	0
H. Mortensen	100	0	0
Dr. L. G. Morton	25	0	0
J. B. G. Muir	10	0	0
L. J. T. Murphy	10	0	0
A. J. Murray	20	0	0
K. J. Neerhut	5	0	0
T. Y. Nelson	50	0	0
G. Newman-Morris	20	0	0
N. C. Newton	50	0	0
R. Nicks	5	0	0
Dr. Jean Oakes	3	3	0
J. A. O'Brien	10	0	0
Late Robert Officer	100	0	0
I. H. Ogilvy	50	0	0
Estate of late P. L. O'Halloran	29	18	5
C. H. Osborn	100	0	0
Pfizer Pty. Ltd. (per K. W. Starr)	100	0	0
L. H. A. Phillips	25	0	0
Sir Hugh Poate	25	0	0
F. J. A. Pockley	105	0	0
Dr. B. J. Pollard	5	0	0
W. J. Pullen	20	0	0
Balcombe Quick	105	0	0
B. K. Rank	100	0	0
A. I. Rhydderch	20	0	0
C. O. F. Rieger	10	10	0
T. E. G. Robertson	60	0	0
H. Roland	100	0	0
T. F. Rose	20	0	0
C. L. Rosefield	10	10	0
F. F. Rundle	10	0	0
Hugh Ryan	100	0	0
S. M. Schreiber	10	0	0
Margery Scott-Young	20	0	0
F. H. Shanasy	21	0	0
Alan Sharp	100	0	0
Dr. L. T. Shea	25	0	0
Dr. M. D. Silberberg (per J. Grayton Brown)	52	10	0
Lorna V. Sisely	20	0	0
W. Sloss	25	0	0
E. Durham Smith	10	10	0
Julian Smith	105	0	0
J. B. Somerset	10	10	0

S. L. Spencer	21	0	0
Dr. R. B. Spiers	25	0	0
Stack & Co. Pty. Ltd. (per K. W. Starr)	105	0	0
R. H. Stanistreet	10	10	0
K. W. Starr	105	0	0
J. Steigrad	20	0	0
C. R. Stephens	10	10	0
A. L. Stephenson	5	5	0
H. H. Stewart	168	5	0
F. N. Street	10	10	0
G. R. Stirling	5	0	0
S. C. Suggit	21	0	0
M. P. Susman	100	0	0
Mrs. M. P. Susman	50	0	0
H. D. Sutherland	10	10	0
N. G. Sutton	50	0	0
T. G. Swinburne	20	0	0
A. C. Thomas	100	0	0
A. C. G. Thomas	100	0	0
P. A. Tomlinson	5	5	0
Dr. L. G. Travers	25	0	0
A. R. Wakefield	50	0	0
Dr. Annie W. Wall	10	10	0
Peter F. Williams	20	0	0
R. C. Willis	25	0	0
Dr. D. R. C. Wilson	5	5	0
Late Sir George Wilson	25	0	0
N. P. Wilson	20	0	0
W. W. Woodward	10	10	0
D. J. Wurth	5	5	0
G. G. Wyllie	10	0	0
N. R. Wyndham	20	0	0

NEW ZEALAND

E. L. Button	£100	0	0
E. Y. Comrie	5	5	0
K. M. Ewen	5	5	0
E. L. Marchant	6	6	0
J. H. North	7	7	0
D. Robb	20	0	0
S. L. Wilson	105	0	0

Repayment of Gordon Craig Scholarships

In response to a suggestion that Gordon Craig Fellows should repay the whole or part of their scholarship in order to provide further such benefits, the following are thanked for their action:—

I. H. Cumberland
J. L. Dowling
I. Monk
K. N. Morris
L. J. T. Murphy
N. C. Newton
W. J. Pullen
T. E. G. Robertson
A. Sharp

DOUGLAS MILLER,
President.

0 0
0 0
0 0
0 0
0 0
5 0
0 0
0 0
0 0
5 0
0 0
0 0

0 0
5 0
5 0
6 0
7 0
0 0
0 0

part
for

t.